Systems biology studies of Aspergilli - from sequence to science

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Systems Biology Studies of Aspergilli — From Sequence to Science

Ph.D. thesis

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Mephistopheles: “Tell me first, without more ado,
Which Faculty appeals to you?”
Student: “I want to be a learned man,
And find out everything I can —
All the whole universe contains,
All about Nature, which Science explains.‘”
Mephistopheles: “Well, you’re on the right road, that’s clear.
But you will find a lot to distract you here!”

Goethe — Faust

Abstract

The recent dawn of the new biological mindset called systems biology has put forth a new way of analyzing and understanding biology. Carried by the notion that no element of a cell is an island, systems biology takes a holistic approach, and attempts to understand life as systems that have co-evolved and not as a haphazardly compiled list of parts. This has been made possible by the so-called genomic revolution — the sequencing of the genomic DNA of a rapidly increasing number of organisms — and the “omic” tecniques following in the wake of the genome projects: metabolomic, proteomic, and transcriptomic to mention a few.

The recent publication of the genome sequences of several filamentous fungi of the *Aspergillus* species (Aspergilli), has, along with the accumulation of years of reductionist studies, been a catalyst for the application of systems biology to this interesting group of fungi. Among the genome sequenced Aspergilli are a known human pathogen (*Aspergillus fumigatus*), a model organism for cellular mechanisms (*Aspergillus nidulans*) and two industrial workhorses (*Aspergillus niger* and *Aspergillus oryzae*).

In the presented work, new analytical and computational tools have been designed and a systems biology approach has been applied to a wide range of issues. These tools include the compilation of data from literature on *A. niger* enzymes to form a re-constructed metabolic network and model of metabolism, allowing assessment of the industrial production potential of metabolites from this fungus. Based on the network, a map of metabolism has been drawn in the notation of biochemistry text books and a web server built that allows the analysis of genome-scale data for a number of *Aspergillus* species.

Further efforts have produced a tri-*Aspergillus* species Affymetrix DNA microarray for expression analysis of the predicted genes of *A. nidulans*, *A. niger* and *A. oryzae*, and a case study of an advanced application of this chip identified a regulatory response conserved through evolution.

In an application of the tools, a multi-disciplinary comparison of two genome sequenced strains of *A. niger* was conducted using sequence analysis, exo-metabolomics, transcriptomics and classical genetics. With a special focus on the traits making one strain a high-yield citric acid producer and the other an efficient glucoamylase producer, a surprising number of co-enhancing factors were found on multiple levels of cellular metabolism.

Transcriptome profiling coupled with metabolic modeling further allowed the charting of the genome-wide regulation of *A. niger* in response to ambient pH in the context of organic acid production and a plausible explanation for the evolution of the capabilities to be a high-yield producer of citric acid. Furthermore, a detailed transcriptome profiling of all of the genes of *A. niger* predicted to code for extracellular enzymes was made using a new literature-based graphical tool for analysis of the degradation targets of the enzymes.

In conclusion, the versatility of a systems biology approach to understanding *Aspergillus* physiology has been demonstrated through a number of studies with results relevant to biotechnological processes.

Dansk resumé

En nyeligt opstået tilgang til biologien — systembiologi — taler for en ny måde at analysere og forstå biologi på. Ud fra en filosofi om at ingen dele af cellen står alene, har systembiologien en holistisk tilgang, og forsøger at forstå livets komponenter som systemer der har udviklet sig i samspil med hinanden snarere end en tilfældigt sammensat liste af komponenter. Det er i høj grad blevet gjort muligt af den såkaldte genomrevolution — sekventeringen af arvemassen i et stærkt stigende antal arter — og "omiske"-teknikker som er opstået i kølvandet af genom-projekterne: metabolomiske, proteomiske, og transkriptomiske, for at nævne nogle få.

Offentliggørelsen af genomsekvensen af flere skimmelsvampe af slægten *Aspergillus* (Aspergilli) har, sammen med årtiers studier med den gængse reduktionistiske tilgang til biologien, katalyseret anvendelsen af systembiologi på denne interessante gruppe af svampe. Blandt de genomsekventerede Aspergilli findes én, som er sygdomsfremkaldende hos mennesker (*Aspergillus fumigatus*), én, som er en modelorganisme for levende cellers udvikling (*Aspergillus nidulans*), og to, der bruges i bio-industrielle processer (*Aspergillus niger* og *Aspergillus oryzae*).

I den nærværende afhandling præsenteres nye analyseværktøjer, som, sammen med en systembiologisk tilgang, har muliggjort analyse af en bred vifte af problemstillinger. Disse værktøjer tæller blandt andet indsamlingen af data om enzymer fra *A. niger* fra litteraturen for at rekonstruere denne svamps stofskifte og modellere dette, og dermed vurdere potentialet for industri-skala produktion af stofskifteprodukter fra denne skimmelsvamp. På baggrund af denne stofskifte-model blev der produceret et kort over metabolismen, og oprettet en internetserver, som letter analysen af data på genom-niveau for et antal *Aspergillus* arter.

Et andet værktøj, som er et produkt af denne afhandling, er et Affymetrix DNA microarray til analyse af hvilke gener er udtrykt i arterne *A. nidulans*, *A. niger* og *A. oryzae*. Et studie, som er et eksempel på de mere avancerede brugsmuligheder af dette array, har identificeret en cellulær reguleringsmekanisme, som er bevaret gennem evolutionen.

I én anvendelse af disse værktøjer blev der udført en multidisciplinær sammenligning af to genom-sekventerede stammer af *A. niger* ved hjælp af DNA sekvensanalyse, transkriptomanalyse, profiler af ekstracellulære stofskifteprodukter og klassisk genetik. Ud fra et særligt fokus på de træk, som gør en stamme til en effektiv producent af citronsyre og den anden en effektiv producent af enzymet glucoamylase, blev der fundet et overraskende antal samvirkende faktorer på flere niveauer af cellens stofskifte.

Studier af transkriptionsprofiler i samklang med stofskiftemodellering tillod desuden en kortlægning af regulering på genom-niveau som funktion af pH-niveauet for *A. niger* i relation til produktionen af organiske syrer og opstillingen af en sandsynlig forklaring for udviklingen af potentialet til produktion af citronsyre i højt udbytte. Derudover blev der lavet detaljerede profiler af alle gener fra *A. niger*, som formodes at kode for extracellulære enzymer, ved hjælp af et nyt litteraturbaseret værktøj til analyse af enzymernes nedbrydningsprofil.

Det er dermed blevet demonstreret i denne afhandling, gennem et antal studier med relevans for bioteknologien, hvor alsidige aspekter af *Aspergillus* fysiologi en systembiologisk tilgang kan belyse.

Preface

> "I was just guessing/At numbers and figures/Pulling your puzzles apart
> Questions of science/Science and progress/Do not speak as loud as my heart"
> *Coldplay — The Scientist*

After three years enjoying the support from my friends and colleagues at work, and after hours by friends and family, it seems a token gesture to spend a few lines here to thank the people that have carried me through my studies. While I will try to the best of my ability to put years of gratitude onto paper, I hope that everyone mentioned here will know that my affection for all of you extends far beyond this preface.

As several people have rightly commented, the course of my Ph.D. studies has in many ways been a lucky streak of meeting the right people at the right time. First among these is my main supervisor professor Jens Nielsen, who from the first time we met, conveyed a great enthusiasm for the project and the prospect of supervising me. With often more confidence in my abilities than myself and a willingness to open doors for a humble student, Jens has with his charisma, dedication to his students, and a combination of optimism and no-nonsense honesty been a role model to me personally and scientifically, and I hope to keep learning from him.

I am also grateful to Jens for assigning me Michael L. Nielsen my co-supervisor. I have felt that Michael has shown a genuine personal interest in me, and has been a solid support through the entire project. Michael is known to everyone around him to be a great instructor, and had the patience to teach me molecular biology of Aspergilli. I am especially grateful for the great dedication and meticulousness he has shown in providing feedback on my written work and especially this thesis, which has taught me a lot about scientific writing and greatly improved the final product. Even so, any poor reasoning and unclarities are entirely my own.

Through Jens I was also put in touch with Scott E. Baker of the Pacific Northwest National Laboratories in Richland, WA, USA, who was kind enough to sponsor a two month research stay in his laboratories. This period was a fantastic time, both personally and research-wise, where I was shown great hospitality from the entire Fungal Biotechnology group, but especially Scott and his family. I will especially remember Scott's weekly delivery of the local delicacy Spudnuts and spending Halloween with Scott and his family. It is a rare gift finding such a thoroughly nice person, and I sincerely hope our collaborations and friendship will continue in the future.

Furthermore, I had the extreme fortune of being offered to supervise two uniquely talented masters students, Malene G. Jakobsen and Linda Lehmann, who each put in a year of dedicated work. Both of them showed a great personal drive and a talent for making good research out of my sometimes only sketchy instructions. Almost every hour of lab work performed by them have produced results directly applicable in the work of this thesis.

I've had the privilege of working in an environment populated with competent technical staff, a helpful administration, and extremely inspiring colleagues of which some have become friends. I especially wish to thank the following: Tina Johansen for excellent technical assistance, Trine Bro for being a great support and assigning tasks with a smile (Jens has got nothing on you in this regard!), Birgitte Karsbøl for always be-

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A number of people have (not necessarily knowingly) made helpful comments on parts of the manuscript or elements of the presented work. For that, I am indebted to (in alphabetical order) Line Albertsen, Mikko Arvas, Randy Berka, Sven Even Borgas, Kenneth Bruno, Robbert Damveld, Ronald de Vries, Jens Frisvad, Igor Grigoriev, Gerald Hofmann, Christian C. Kubicek, Linda L. Lasure, Linda Lehmann, Frederik Lundberg, Diego Martinez, Kevin McCluskey, Uffe Mortensen, José Manuel Otero, Herman Pel, Miguel Peñalva, Peter Punt, Peter Schaap, Peter J.I. van de Vondervoort, Hans van den Brink, and Jaap Visser.

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Finally, I am convinced that this thesis would never have been started or finished without the love of my wife Maria and our daughter Lærke. For you, all the words of thanks and love I could write would be too few, yet none of them would be powerful enough. To you, I dedicate every word of this work and the rest of my life.

Mikael Rørdam Andersen
Copenhagen, Denmark
November 2008

Publications

> **Calvin:** "I realized that the purpose of writing is to inflate weak ideas, obscure poor reasoning, and inhibit clarity. With a little practice, writing can be an intimidating and impenetrable fog! [...] Academia, here I come!"
> *Bill Watterson's Calvin & Hobbes*

The results presented in this thesis have formed the basis of the following articles, book chapters and manuscripts:

Andersen MR, Salazar M, Schaap PJ, van de Vondervoort PJI, Culley D, Thykær J, Frisvad JC, Nielsen KF, Albang R, Albermann K, Berka RM, Dai Z, Hofmann G, Lasure LL, Magnusson JK, Meijer SL, Nielsen JB, Nielsen ML, van Ooyen AJJ, Panther K, van Dijck PWM, van Peij NNME, Pel HJ, Samson RA, Stam H, Tsang A, van den Brink H, Shapiro H, Schmutz J, Pangilinan J, Salamov A, Lou Y, Lindquist E, Grimwood J, Grigoriev I, Kubicek CP, Martinez D, Nielsen J, Roubos JA, Baker SE. A Snapshot of Evolution: *Aspergillus niger* ATCC 1015 versus CBS 513.88. (Manuscript in preparation).

Andersen MR, Kjeldsen K, Nookaew I, Vongsangnak W, Nielsen J. ReMapper: A genome-scale model-based tool for analysis of systemic data in industrially relevant microorganisms. (Manuscript in preparation).

Andersen MR, Jakobsen MG, de Vries RP, Nielsen J. Network-based analysis of carbohydrate-active gene transcription in *Aspergillus niger*. (Manuscript in preparation).

Andersen MR, Lehmann L, Nielsen J. A systems-wide approach to understanding organic acid production in *Aspergillus niger*. (Submitted).

Andersen MR, Nielsen J. Current status of systems biology in Aspergilli. *Fungal Gen Biol*, 2008 (In press).

Andersen MR, Vongsangnak W, Panagiotou G, Salazar MP, Lehmann L, Nielsen J. A trispecies *Aspergillus* micro array: comparative transcriptomics of three *Aspergillus* species. *Proc Natl Acad Sci U S A*, 105(11):4387–4392, 2008.

Andersen MR, Nielsen ML, Nielsen J. Metabolic model integration of the bibliome, genome, metabolome and reactome of *Aspergillus niger*. *Mol Syst Biol*, 4:178, 2008.

Andersen MR, Rueksomtawin K, Hofmann G, Nielsen J. Metabolic Engineering of Filamentous Fungi. In: Metabolic Pathway Engineering Handbook. Tailor and Francis Group, LLC.(In press)

Furthermore, the work presented in this thesis has provided minor contributions to the following articles and manuscripts:

Salazar M, Vongsangnak W, Panagiotou G, **Andersen MR**, J. Nielsen. Uncovering transcriptional regulation of glycerol metabolism in aspergilli through genome-wide gene expression data analysis. (Manuscript in preparation).

Tsang A, Zerbs S, Collart FR, Magnusson JK, **Andersen MR**, S.E. Baker SE. A bioinfor-

matic comparison of glycosyl hydrolases from two strains of *Aspergillus niger*. (Manuscript in preparation).

Meijer SM, Otero JM, Hernandez RO, **Andersen MR**, Nielsen J, Olsson L. Creation of a cytosolic reductive TCA cycle in *Aspergillus niger* — Heterologous gene insertion of fumarase and fumarate reductase. (Manuscript in preparation).

Meijer SM, Otero JM, Hernandez RO, **Andersen MR**, Nielsen J, Olsson L. Overexpression of isocitrate lyase — Glyoxylate bypass influence on metabolism in *Aspergillus niger*. (Manuscript in preparation).

Panagiotou G, **Andersen MR**, Grotkjaer T, Regueira TB, Hofmann G, Nielsen J, Olsson L. Development of a platform for the expression of fungal polyketides in *Aspergillus nidulans*. *Appl Environ Microbiol*, (Submitted).

Panagiotou G, **Andersen MR**, Grotkjaer T, Regueira TB, Hofmann G, Nielsen J, Olsson L. Systems analysis unfolds the growth effects of the phosphoketolase pathway in *Aspergillus nidulans*. *PLoS One*, 2008 (In press).

Coutinho P, **Andersen MR**, Kolenova K, vanKuyk PA, Benoit I, Gruben BS, Trejo-Aguilar B, Visser H, van Solingen P, Pakula T, Seiboth B, Battaglia E, Aguilar-Osorio G, de Jong JF, Ohm RA, Aguilar M, Henrissat B, Nielsen J, Stålbrand H, de Vries RP. Post-genomic insights into the plant polysaccharide degradation potential of *Aspergillus nidulans* and comparison to *Aspergillus niger* and *Aspergillus oryzae*. *Fungal Gen Biol*, 2008 (In press).

Thykaer J, **Andersen MR**, Baker SE. Pathway Identification: From *in silico* analysis to antifungal targets in *Aspergillus fumigatus*. *Med Mycol*, 2008 (In press).

Pel HJ, de Winde JH, Archer DB, Dyer PS, Hofmann G, Schaap PJ, Turner G, de Vries RP, Albang R, Albermann K, **Andersen MR**, Bendtsen JD, Benen JA, van den Berg M, Breestraat S, Caddick MX, Contreras R, Cornell M, Coutinho PM, Danchin EG, Debets AJ, Dekker P, van Dijck PW, van Dijk A, Dijkhuizen L, Driessen AJ, d'Enfert C, Geysens S, Goosen C, Groot GS, de Groot PW, Guillemette T, Henrissat B, Herweijer M, van den Hombergh JP, van den Hondel CA, van der Heijden RT, van der Kaaij RM, Klis FM, Kools HJ, Kubicek CP, van Kuyk PA, Lauber J, Lu X, van der Maarel MJ, Meulenberg R, Menke H, Mortimer MA, Nielsen J, Oliver SG, Olsthoorn M, Pal K, van Peij NN, Ram AF, Rinas U, Roubos JA, Sagt CM, Schmoll M, Sun J, Ussery D, Varga J, Vervecken W, van de Vondervoort PJ, Wedler H, Wösten HA, Zeng AP, van Ooyen AJ, Visser J, Stam H. **Genome sequencing and analysis of the versatile cell factory *Aspergillus niger* CBS 513.88**. *Nature Biotechnology*, 25(2):221–231, 2007.

Abbreviations

Abbreviations for the 1045 metabolites of the model presented in chapter 3 have been excluded from this list. They may be found in App. Table A.2.

2D-PAGE Two-dimensional polyacrylamide gel electrophoresis

AIST National Institute of Advanced Industrial Science of Technology (Japan)

bp Base pairs

C_2 Two-carbon (compound)

C_3 Three-carbon (compound)

C_4 Four-carbon (compound)

C_5 Five-carbon (compound)

CADRE Central *Aspergillus* data repository

CBD Carbohydrate-binding domain

CDS Coding sequences

DAD Diode array detector

diMS Direct infusion mass spectrometry

DOE Department of Energy

EC Enzyme Commission

EMP Embden-Meyerhoff-Parnas

ER Endoplasmatic reticulum

EST Expressed sequence tag

FBA Flux balance analysis

FCC Flux control coefficients

FGI Fungal Genome Initiative

FGSC Fungal Genetics Stock Center

GABA γ-aminobutyrate

GC-MS Gas chromatography-mass spectrometry

GC-TOF Gas chromatography-time-of-flight mass spectrometry

GEO Gene Expression Omnibus

GOLD Genomes OnLine Database

GPI Glycosylphosphatidylinositol

GRAS Generally regarded as safe

HPLC High performance liquid chromatography

HR-MS High resolution mass spectrometry

JCVI J. Craig Venter Institute

JGI Joint Genome Institute

KOGs Eukaryotic orthologous groups

LC Liquid chromatography

LC-MS Liquid chromatography-mass spectrometry

Mb Megabases

MCA Metabolic control analysis

MFA Metabolic flux analysis

MM Minimal medium

MS Mass spectrometry

mtDNA Mitochondrial DNA

NCBI National Center for Biotechnology Information (USA)

NITE National Institute of Technology and Evaluation, Japan

NRPS Non-ribosomal peptide synthase

OOPS One occurrence per sequence

ORF Open reading frame

PBS Phosphate buffered saline

PCA Principal component analysis

PDA Potato dextrose agar

PDF Portable document format

PFGRC Pathogen Functional Genomics Resource Center

PKS Polyketide synthase

PP Pentose phosphate

PPP Pentose phosphate pathway

PS Post script

RMA Robust multiarray average

SFL Summed fractional labeling

SHAM Salicylhydroxamic acid

SVG Scalable vector graphics

TCA Tri-carboxylic acid (cycle)

TCM Two-component-mixture

TIGR The Institute for Genomic Research

UTR Untranslated region

vvm Volume of gas per volume of liquid per minute

WGS Whole-genome shotgun

ZOOPS Zero or one occurrence per sequence

Nomenclature

μ Specific growth rate

μ_{max} Maximum specific growth rate

$\mathbf{c}$ Row vector containing the influence of individual fluxes on the objective function z

m_{ATP} ATP requirement for non-growth associated activities (maintenance)

m Number of metabolites

n Number of reactions or fluxes

$\mathbf{S}$ stoichiometric matrix

$\mathbf{v}$ Flux activities for all metabolic reactions

q_s Substrate consumption rate

Y_{xATP} ATP cost of growth-associated maintenance

z objective function

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Chapter 1

Introduction

> **Calvin:** "I think we have got enough information now, don't you?"
>
> **Hobbes:** "All we have is one "fact" that you made up."
>
> **Calvin:** "That's plenty. By the time we add an introduction, a few illustrations and a conclusion, it'll look like a graduate thesis."
>
> *Bill Watterson's Calvin & Hobbes*

The work presented in this thesis was performed between April 2005 and April 2008 under the Ph.D. program of Chemistry and Biotechnology at the Technical University of Denmark. The work was supervised by professor Jens B. Nielsen and postdoctoral researcher Michael L. Nielsen. Funding was provided by the Danish Research Agency for Technology and Production.

The aim of this thesis was to investigate several physiological and genetical traits of Aspergilli by constructing and applying systems biology models and analysis tools. While the work covers many areas, a particular focus area was traits relevant to biotechnological processes. Most of the presented work is on aspects of the physiology of *Aspergillus niger*, but analyses of *A. fumigatus*, *A. nidulans* and *A. oryzae* physiology and genetics have been conducted as well.

1.1 The structure of the thesis

To provide context for the work presented in the following chapters, **chapter 2** provides a general introduction to the work by presenting a comprehensive review of the systems biology and genome-scale ("omics") work that have been reported in the Aspergilli. Furthermore, to reflect the industrial focus and the possible applications of the results, the chapter also contains a review of the metabolic engineering efforts of biotechnological processes that apply *Aspergillus* species.

Chapter 3 presents a genome-scale stoichiometric model of the metabolism of *A. niger*. The model was constructed by a literature-based bottom-up approach to include as many aspects of the metabolism of *A. niger* as possible. The chapter includes the application of the model to predict mechanisms of high-yield acid production and theoretical maximum yields of commercial products.

In **chapter 4**, a web-based software tool for aiding the analysis of genome-scale data in the context of metabolism is presented. The tool is an application of maps of the metabolic network that was reconstructed in chapter 3, and is used for the analysis and presentation of the data generated in several of the following chapters.

Chapter 5 presents the design strategy and key statistics of a custom Affymetrix GeneChip with probes for the predicted genes of *A. nidulans* A4, *A. niger* ATCC 1015 and *A. oryzae* RIB40. The validation of the chip and an example of its use for inter-species comparative transcriptomics is presented in **chapter 6**. The results of this chapter describe common evolutionary traits in the group of Aspergilli, specifically the response to D-xylose in the medium, which

was found to be mediated by the xylanolytic regulator XlnR in all three species by conserved promoter motifs.

The genomics of *A. niger* are interesting in the context of biotechnology, as both a high-yield citric acid producer and a high-yield enzyme-producing strain have been whole-genome sequenced. The work of **chapter 7** is a presentation of the genome of the acidogenic strain as well as a comparison of the two strains at multiple levels, from genomics over transcriptomics to exo-metabolism, to elucidate traits separating the two strains. This has resulted in the identification of systems-level traits defining either type of strain. These traits identify targets for future engineering efforts.

Chapter 8 is a more detailed study of the mechanisms of acidogenesis in *A. niger* by an extension of the model presented in chapter 3, where it is shown that the pH-triggered acid production of citrate and oxalate corresponds with the pH-intervals where each acid is the most efficient at acidifying the environment. Furthermore, transcriptional profiling across three levels of pH allowed for the prediction of pH-dependent cis-acting promoter elements as well as support for a comparative genomics study of the presence of the pH-responding *pel/pacC* signal transduction pathway.

An in-depth analysis of carbon source-based regulation of the transcription of genes coding for carbohydrate-active enzymes is presented in **chapter 9**. The results include a comprehensive overview of the literature on the enzymatic degradation of poly-saccharides by *A. niger* and an extension of the mapping software of chapter 4, allowing the interpretation of transcription profiles of genes in the context of the polysaccharide structures that the enzymes encoded by the genes degrade.

Finally, **chapter 10** contains conclusions and perspectives of the research results of the thesis.

1.1.1 Comments

The thesis has been written in a structure similar to a monograph rather than a collection of published and unpublished research articles. This was done in the hope of increasing the readability of the content. Published articles and submitted manuscripts are included as separate chapters or parts of these, but the published work has been adapted for the thesis in a number of ways — such as extra text to elaborate on points that the journal formats did not allow. Also, the introductory sections have been modified to put the work into the context of the thesis and to avoid the variations on the same theme that often found in introductions to articles on the same topic. The thesis is however not quite similar to a typical monograph in structure, as the chapters were chosen to be self-contained with materials and methods. This generates somewhat of a redundancy in the methods sections (even though small differences exist from chapter to chapter), but hopefully it increases the readability of the individual chapters.

Throughout the thesis, there are references to data tables that are found only on a web page (`www.computationalbiology.dk`) and not in the appendices. For information that has not yet been published in a scientific journal, the access is given on request. This approach is rather uncommon, and breaks with the principle that a thesis should be contain all the information required for evaluating the research. Even so, it was employed in cases where the table contains a large amount of data that is not useful in a printed format, but of great use in a digital format and should be evaluated in this form (e.g. a table containing information on all genes of a single *Aspergillus* species). It is my hope that the readers will appreciate the choice of functionality before formality. Furthermore, a number of the figures of the appendices of the thesis are very large (up to 2.4×1.8 meters), and are thus not well represented in the scaled print-version. All figures have thus been made available from the web page mentioned above in addition to the printed version.

As the reader will have observed by now, I have added other bits of informality to the thesis in the form of quotes from literature, plays and music that I have been exposed to during the project period, and that I felt added some perspective to the work of the individual chapters. It is my hope that these quotes will sustain the reader through the thesis as the original works sustained me through the course of my Ph.D. studies.

Chapter 2

Application of systems biology to Aspergilli

> "Science, as actually practised, is a complex dialogue between data and preconceptions."
> *Stephen Jay Gould — Wonderful Life*

The *Aspergillus* genus of filamentous fungi has a long history as work horses in the service of human kind. *A. oryzae* (koji mold) was first utilized for the preparation of fermented Asian foods such as shoyu (soy sauce), miso and sake in China almost 2000 years ago (Baker and Bennett, 2007). However, the modern well-defined industrial production of specific compounds was spurred in 1894 by the Japanese-American Jockichi Takamine. Takamine used cultures of *A. oryzae* to produce a complex mixture of enzymes sold as Takadiastase (Hjort, 2003). Since then, the fermentation industry has expanded, and Aspergilli are now being used to produce a wide range of commercially available products from simple organic acids in *A. niger*, through more complex molecules such as statins produced by *A. terreus*, and to polypeptide production in several *Aspergillus* species. For a number of these products, filamentous fungi dominate the market as production hosts (Nevalainen et al., 2005).

Genetics in Aspergilli was initiated in the 1950s, where a now classical paper by Pontecorvo (1953) suggested the use of *A. nidulans* as a model fungus. The study of *A. nidulans* has advanced the understanding of eukaryotic cellular physiology and in many ways been the source of genetics tools used in all Aspergilli. Recent examples of this are gene-targeting with bipartite substrates (Nielsen et al., 2006), and the *ku70* deletion system for improved gene targeting (Nayak et al., 2006). Advancing our knowledge on these fungi as individual species and as a group holds interest to both fundamental biological sciences and applied biotechnology.

To serve as a background for the work presented in this thesis, overviews of metabolic engineering studies and systems biology conducted in filamentous fungi of the genus *Aspergillus* will be provided in this chapter. There are several different definitions of metabolic engineering, but here the definition of Bailey (1991) will be used, who defined metabolic engineering as "the improvement of cellular activities by manipulations of enzymatic, transport, and regulatory functions of the cell with the use of recombinant DNA technology". Examples of all these types of directed changes in the cells will be presented in this chapter. Even so, as several of the examples of metabolic engineering described in this review chapter will make clear, the robustness of the cellular machinery is a challenge for the successful use of directed genetic modifications. Redundancies and complex circuitries within the cell often counteract the modifications — as discussed by Friboulet and Thomas (2005). Additionally, regulation can occur at the transcriptomic, proteomic and metabolomic level, and a more holistic view than

the traditional metabolic engineering strategy is therefore often required. For this reason, the use of a system-based approach to metabolic engineering is gaining ground.

Traditionally, the only technique capable of making changes on a systems-wide level, was the use of classical strain improvement through mutagenesis and screening. However, this is an indirect approach, and the changes are difficult to identify and interpret. Use of a systems-wide approach assists in identifying features for engineering, while still taking the complexity of the system into account. By the use of several different "omic" techniques, the appearance of large datasets and the use of mathematical modeling, one may hope to accumulate a critical mass of knowledge that allows new hypotheses on the system to be put forth, and thereby suggesting a strategy for the metabolic engineer.

Additionally, several studies have been published in recent years using systems-wide techniques in Aspergilli, which are either applied to metabolic engineering purposes or provides techniques relevant for these applications. The sudden burst in available fungal genomes (Nierman et al., 2005, Machida et al., 2005, Galagan et al., 2005, Pel et al., 2007, Fedorova et al., 2008) makes the system-wide approach even more appealing for the future. For these reasons, it has been chosen to include sections on genomics, transcriptomics, proteomics, metabolomics and modeling studies in Aspergilli. In many of the applications, this work shows the possibilities and potential of systems biology, and the perspectives of developing new platforms and tools.

2.1 System-wide approaches

2.1.1 Genomics

Even though genome sequencing projects for *A. nidulans* and *A. oryzae* started as early as 1998 and 1996, respectively, the genomics era of filamentous fungi is generally agreed to have started in February 2001, when the Whitehead Institute Center for Genome Research released a draft version of the genome sequence of *Neurospora crassa*. The finished version of the genome sequence was published in 2003 (Galagan et al., 2003). As a testament to the importance of the work, a 107 page review of the impact of the *N. crassa* genome sequence was published by Borkovich et al. (2004).

In this chronology, *Aspergillus* genomics thus started in January 2003, where full public access to a threefold(3x) coverage *A. nidulans* genome sequence from Cereon genomics (Archer and Dyer, 2004). Two months later, this sequence was re-released by the Whitehead Institute/MIT Center for Genome Research with the addition of a 10x coverage sequence to generate a genome sequence with 13x coverage. Similarly, the Dutch company DSM announced the genome sequencing of an enzyme-producing strain of *A. niger* in a press release in December 2001, but restricted access to collaborators. A publication on the *A. nidulans* genome sequence was released in December 2005 along with publications on the genome sequence of *A. oryzae* and the opportunistic pathogen *A. fumigatus*, the primary agent behind invasive aspergillosis, the most frequent fungal infection in the world (Galagan et al., 2005, Machida et al., 2005, Nierman et al., 2005), while the genome sequence of *A. niger* CBS 513.88 was made accessible to the public along with the publication of Pel et al. (2007).

Several *Aspergillus* genomes have been sequenced in parallel with or during the milestone publications of these four genomes, some by independent agencies, other as part of community efforts. One such effort is the Fungal Genome Initiative (FGI) (`http://www-genome.wi.mit.edu/seq/fgi/`) that since 2002 has released white papers suggesting fungi to be sequenced, including the 10x sequencing of *A. nidulans* which was a part of the proposal of the first white paper (Fungal Genome Initiative, 2002). So far four white papers have been released suggesting the sequencing of a total of 99 fungal species, including eight Aspergilli. Table 2.1 summarizes the current number of whole-genome sequencing projects from Aspergilli. These include the Aspergilli described above, as well as the following:

Aspergillus aculeatus Plant pathogen also used for identification of new extracellular

Table 2.1: Overview of whole genome sequence projects for *Aspergillus* species. The data was compiled from Jones (2007), the NCBI genome project webpage and Genomes OnLine Database (GOLD, http://www.genomesonline.org)

Species	Strain	Sequencing agency	Contigs	Coverage (Fold)	Gene models	Size (Mb)	Publication
A. aculeatus	ATCC 16872[a]	DOE Joint Genome Institute	N/A	N/A	N/A	N/A	S.E. Baker, pers. comm.
A. carbonarius	IMI 388653[a]	DOE Joint Genome Institute	N/A	N/A	N/A	N/A	S.E. Baker, pers. comm.
A. clavatus	NRRL 1	TIGR[b]	231	11.4	9125	27.86	Fedorova et al. (2008)
A. (Neosartorya) fischeri	NRRL 181	TIGR[b]	1067	N/A	10,437	32.55	Fedorova et al. (2008)
A. flavus	NRRL 3357	TIGR[b]	3388	10	13,071	36.3	Yu et al. (2005)
A. fumigatus	Af293	TIGR[b]/Sanger Institute	19	10.5	9887	29.4	Nierman et al. (2005)
A. fumigatus	A1163	TIGR[b]/Celera Genomics /Merck & Co, USA.	140	N/A	10,099	29.2	Fedorova et al. (2008)
A. (Emericella) nidulans	FGSC A4	Broad Institute	248	13	10,701	30.06	Galagan et al. (2005)
A. niger	CBS 513.88	DSM, The Netherlands	498	7.5	14,165	33.9	Pel et al. (2007)
A. niger	ATCC 9029	Integrated Genomics	9510	4	N/A	N/A	
A. niger	ATCC 1015	DOE Joint Genome Institute	24	8.9	11,200	34.9	Baker (2006)[c]
A. oryzae	RIB40	NITE	24	9	12,074	37	Machida et al. (2005)
A. parasiticus	Unknown[a]	University of Oklahoma	N/A	N/A	N/A	N/A	
A. terreus	ATCC 20542	Microbia	N/A	N/A	N/A	N/A	
A. terreus	NIH 2624	Broad Institute	267	N/A	10,406	29.3	

[a] Not yet released
[b] TIGR is now a part of the J. Craig Venter Institute
[c] This publication is not formally the genome analysis publication, which is in preparation (see chapter 7), but is often used as a reference.

enzymes as in the study by Dalbøge (1997), where interesting genes were cloned from cDNA and expressed in *A. oryzae*.

Aspergillus carbonarius Ochratoxin producer and involved in food spoilage, particularly of grapes. It is closely related to *A. niger* and the other black Aspergilli.

Aspergillus clavatus Allergenic and rarely pathogenic fungus that is primarily being sequenced to gain a further understanding of the two closely related pathogenic Aspergilli *A. fumigatus* and *A. terreus*.

Aspergillus (Neosartorya) fischeri Non-pathogenic close relative to the pathogenic *A. fumigatus*.

Aspergillus flavus Human pathogen producing the highly carcinogenic aflatoxin. It also causes economic losses due to grain infections.

Aspergillus parasiticus A producer of aflatoxin.

Aspergillus terreus Used industrially to produce the cholesterol lowering agents pravastatin, simvastatin, and lovastatin and the organic acid itaconic acid (Bonnarme et al., 1995, Manzoni and Rollini, 2002), but has also been connected with aspergillosis (Birren et al., 2004).

As the list of Table 2.1 continues to grow, so does the need for organization. Resources like the Broad Institute *Aspergillus* comparative database (http://www.broad.mit.edu/annotation/genome/aspergillus_group/MultiHome.html), e-fungi (http://www.cs.man.ac.uk/~cornell/eFungi/database.html), and the central *Aspergillus* data repository (CADRE) (http://www.cadre-genomes.org.uk/ (Mabey et al., 2004), designed for the comparison of genomic data, will arguably be of even greater importance to researchers as the number of whole-genome sequenced Aspergilli increases and allows for more studies based on comparative genomics.

The original four mile-stone genome papers have catalyzed a wide range of genome-driven work, as can be reflected in a planned special

issue of Studies in Mycology (no. 59) on "*Aspergillus* systematics in the genomic era", as well as an issue of Fungal Genetics and Biology planned to be released in the late summer of 2008. As an overview of the status and potential of the genome-driven approach, the following sections will outline research on genomics in *Aspergillus* species, where such has been published. In the context of fungi, a recent definition of genomics has been "the determination and use of the genome sequence of organisms to identify genes and non-coding, but potentially functionally important, regions of the genome" (Archer and Dyer, 2004, Hofmann et al., 2003). The present overview will focus on this type of studies, such as the publications on whole-genome sequencing or genome surveys; however a few examples of systems-wide functional genomics or comparative genomics will be included to provide perspectives of genomics.

Aspergillus aculeatus genomics

The genome sequence of *A. aculeatus* is still in the sequencing and annotation pipeline of the JGI (Scott Baker, personal communications), and no study of genomics or the perspectives of these have been released at this time.

Aspergillus carbonarius genomics

As with *A. aculeatus*, the genome sequence of *A. carbonarius* has not yet been released from the JGI (Scott Baker, personal communications). Studies have been limited to a comparative study of the mitochondrial genome of different *A. carbonarius* strains has been published by Hamari et al. (1999), but it is based mainly on restriction mapping, and not on genome sequence.

Aspergillus clavatus genomics

The genome sequence of *A. clavatus* strain NRRL 1 has recently been published by Fedorova et al. (2008) along with the genome sequences of *N. fischeri* and a second strain of *A. fumigatus*, and is available from NCBI in its third version. Research in the fungus is rather sparse compared to other Aspergilli, and the contributions based on nucleotide sequence are limited to the cloning of clavin by Parente et al. (1996). Wortman et al. (2006) have anticipated that comparative genomics of *A. clavatus*, *A. fischeri*, and *A. fumigatus* will allow the identification of factors responsible for pathogenicity in *A. fumigatus*. Pathogenicity was indeed one of the objects of study in the genome paper by Fedorova et al. (2008) and will be discussed in more detail in the section on *A. fumigatus* genomics.

Neosartorya fischeri genomics

The genome sequence of the eight chromosomes of *N. fischeri* has been analyzed and compared to the genomes of *A. clavatus* NRRL 1, *A. fumigatus* A1163, and *A. fumigatus* Af293 in the work by Fedorova et al. (2008).

Aspergillus flavus genomics

A preliminary commentary on the publication of the *A. flavus* genome has been published by Yu et al. (2005), marking the availability of the sequence information. While the article does not contain the genomic analysis found in the publications of *A. fumigatus*, *A. nidulans*, *A. niger*, and *A. oryzae*, aflatoxin biosynthesis and the aflatoxin gene cluster were mentioned as targets of special interest for future analysis. This has indeed been been analyzed further, as will be described in the section on transcriptomics.

Aspergillus fumigatus genomics

The sequencing of *A. fumigatus* Af293 was initiated in 2001, and a commentary was published by Denning et al. (2002), describing the anticipation of how the project would fuel research in antifungal drugs. The annotation and analysis of a 922 kb large region was published by Pain et al. (2004), allowing the early identification of factors putatively involved in pathogenicity and antifungal targets. However, this study was superseded by the publication of the analysis of the full genome sequence by Nierman et al. (2005), where the genome was examined for allergens and features that may be involved in pathogenicity. These analyses predicted nine proteins to be allergens, and identified 26 clusters that may be

involved in the production of secondary metabolites.

Furthermore, a derivative of the clinical isolate strain *A. fumigatus* CEA10, *A. fumigatus* FGSC A1163, has been sequenced by Merck & Co and was subject to a preliminary analysis by Wortman et al. (2006) and a comparative analysis of *A. fumigatus* FGSC A1163 and *A. fumigatus* Af293 by Rokas et al. (2007). In the recent publication of the genome sequence of *A. fumigatus* FGSC A1163 along with the sequences of *A. clavatus* NRRL 1 and *N. fischeri* NRRL 181, the genome sequences were compared to identify genomic elements unique to *A. fumigatus* FGSC A1163, and to *A. fumigatus*, thus providing potential targets for further study of the cause of pathogenicity.

The research spurred by the genome sequence of *A. fumigatus* Af293 covers many aspects, as was described in a review by Ronning et al. (2005), focusing on a wide range of characteristics and comparative genomics to *A. nidulans* and *A. oryzae*. One use of the genome sequence in the context of basic research was the identification of mating-type-like genes in the asexual *A. fumigatus* (Pöggeler, 2002, Firon et al., 2002, Varga, 2003) (reviewed by Dyer et al. (2003)). The two mating types were finally confirmed by Paoletti et al. (2005), thereby suggesting an active sexual cycle. A review of the impact of the genome sequence of pathogenic fungi as well as identification of more putative pathogenic gene clusters has been put forth by Bowyer and Denning (2007).

Aspergillus nidulans genomics

As described in the introduction to *Aspergillus* genomics above, the genome sequencing of *A. nidulans* FGSC A4 was initiated by Cereon Genomics (Monsanto) in 1998 with the public release of the genome sequence in June 2003. After two years of annotation and research efforts, the genome paper by Galagan et al. (2005) was published. The *A. nidulans* genome was originally predicted to contain 9,541 protein coding genes, but after an extensive manual curation of the gene predictions in March 2006, the number of predicted genes was revised to 10,701.

A recent paper by David et al. (2008) uses genomics as well as metabolic pathway reconstructions to provide functional assignments to 472 orphan genes.

Aspergillus niger genomics

A. niger CBS 513.88 was the first of so far three *A. niger* strains to be whole-genome sequenced. The genome sequencing was initiated by the Dutch company DSM in cooperation with Gene Alliance in July 2000, and was reported by DSM to be finished in December 2001. The strain is a progenitor of the industrial glucoamylase-producing strains currently in use and the genome sequence was analyzed by Pel et al. (2007). A major contribution of this genome publication was the annotation of a number of commercially relevant enzymes, including more than 200 putative proteases and approximately 170 hypothetical and previously characterized carbohydrate-active enzymes.

The second *A. niger* genome sequence is of *A. niger* ATCC 9029, an often used lab-strain. The genome was sequenced by Integrated Genomics and released in 2005 as a heavily fragmented (9510 contigs) draft sequence without annotation or gene predictions.

Finally, the Joint Genome Institute (JGI) under the funding support from the US Department of Energy (DOE) has completed and released the genome sequence of *A. niger* ATCC 1015, a citric acid producer originally described in 1917. An analysis of the genome sequence and a comparison to the CBS 513.88 strain is presented in chapter 7. The publication of Baker (2006) was the first using and presenting the *A. niger* ATCC 1015 genome sequence, and will in this thesis be used as a reference for this sequence, although it is not formally a publication of the genome sequence.

Other genomics performed in *A. niger* includes the sequencing of 12,820 expressed sequence tags (ESTs) by Semova et al. (2006) with the prediction of 5108 genes. This survey of the expressed genes provides a valuable resource that has value both separately and in conjunction with an available genome sequence. Furthermore, Juhász et al. (2008) sequenced the complete genome sequence of the 1a mitochondrial DNA (mtDNA) type of *A. niger* and

2b mtDNA type of *Aspergillus tubingensis* and found the two mtDNAs to be almost identical.

The value of a genome sequence for an industrially relevant species has been demonstrated by DSM, where it has been used in product development. Examples include a protease product called "Brewer's Clarex" that prevents chill-haze in beer (Lopez and Edens, 2005), a protease product to eliminate bitterness of protein supplement sport drinks (Edens et al., 2005), and "PreventASe", an asparaginase product aimed at reducing acrylamide formation in baked and fried foods (DSM Food Specialities, 2007).

Aspergillus oryzae genomics

While the whole genome sequencing of *A. oryzae* RIB40 was initiated in 1996 (Machida, 2002), the complete genome sequence was not publicly released until 2005. The genome paper by Machida et al. (2005) analyzed the genome and the predicted genes. An interesting finding is that compared to *A. fumigatus* and *A. nidulans*, the *A. oryzae* genome seems to have been enriched for genes involved in metabolism. Many of the enriched traits seem to be at least partially due to its long history of food production. A detailed review by Kobayashi et al. (2007) describes recent results of a number of genomics and functional genomics efforts.

The *A. oryzae* genome has special interest for enzyme processing of food stuffs, and as a parallel example to the *A. niger* asparaginase PreventASe described above, an *A. oryzae*-derived enzyme of a similar function and efficiency has been launched by Novozymes A/S under the name AcrylAway (Novozymes, 2007).

Aspergillus parasiticus genomics

A cosmid-based sequencing of the *A. parasiticus* genome has been undertaken by the University of Oklahoma. While the sequencing is still in progress, the first two cosmids (more than 70 kb of sequence in total) have been released to NCBI (Accession numbers AC005991 and AC007872).

Aspergillus terreus genomics

The sequencing of *A. terreus* was suggested in February 2002 in the first white paper by FGI due to its commercial relevance. Another white paper by Birren et al. (2004) emphasized the potential in comparative analysis with the genomes of other pathogenic Aspergilli such as *A. clavatus*, *A. fischerianus*, and *A. fumigatus* to improve the understanding of fungal evolution and pathogenesis.

In August 2005, the sequence of the clinical isolate strain NIH 2624 was released by the Broad Institute complete with automatic annotation, but no analysis of the sequence has been published so far.

Furthermore, the genome sequence of one of the *A. terreus* industrial strains is in the process of being sequenced by Microbia (now Ironwood Pharmaceuticals). No details on this project are readily available, but the clone library was applied in the work by Askenazi et al. (2003), which will be described in detail in the section on transcription analysis.

2.1.2 Transcriptomics

The free accessibility of the genome sequences has resulted in several transcriptome studies of Aspergilli. Since microarrays for expression analysis of Aspergilli have not yet been designed by commercial companies, the research is mainly driven by the efforts of university research groups that design arrays and often make the technology available to other researchers. An overview of the different platforms that have been made available for transcription studies in Aspergilli as well as a comprehensive list of the studies using these arrays are found in Table 2.2.

As this table indicates, at least 34 examples of *Aspergillus* transcriptomics have been published. In addition, several studies based solely on EST sequencing have been reported, the first as early as 1996 (Lee et al., 1996). Examples of distinct types of studies will be presented in more detail. The main groupings of transcriptional studies are the use of microarrays for annotation of gene functions (functional genomics), studies of carbon flow regulation, EST database mining for new gene targets, elucida-

Table 2.2: Overview of *Aspergillus* transcriptome studies and microarray formats. The percentage of the predicted gene models from the genome that are included on the microarray is shown.

Species	Gene models (%)	Type	References
A. nidulans	19.4	cDNA	Sims et al. (2004b,a), Pocsi et al. (2005)
A. nidulans	26.0	cDNA	Malavazi et al. (2006)
A. nidulans[a]	79.0	oligo	Malavazi et al. (2007), Breakspear and Momany (2007)
A. nidulans	89.2	Nimblegen	Bok et al. (2006)
A. nidulans	30.6	Febit	Mogensen et al. (2006)
A. nidulans	16.7	cDNA	Ray et al. (2004)
A. nidulans	26.1	cDNA	Sims et al. (2005)
A. nidulans	88.3	Nimblegen	David et al. (2006, 2008)
A. nidulans	99.6	Affymetrix	Andersen et al. (2008b)[b]
A. niger[c,d]	100.0	Affymetrix	MacKenzie et al. (2005), Martens-Uzunova et al. (2006), Levin et al. (2007a), Pel et al. (2007), Guillemette et al. (2007), Yuan et al. (2008a,b)
A. niger[d]	99.3	Affymetrix	Andersen et al. (2008b)[b]
A. fumigatus	96.2	oligo	Nierman et al. (2005)[e] Sheppard et al. (2005), da Silva Ferreira et al. (2006), Perrin et al. (2007)
A. oryzae	16.8	cDNA	Maeda et al. (2004)
A. oryzae	24.4	cDNA	Masai et al. (2006)
A. oryzae	97.7	Nimblegen	Kimura et al. (2008)
A. oryzae	99.7	Affymetrix	Andersen et al. (2008b)[b]
A. oryzae	89.1	oligo	Tamano et al. (2008)
A. oryzae	98.6	oligo	`www.fermlab.com`[f]
A. flavus[g]	39.7	oligo	Yu et al. (2007)[e], Price et al. (2006), O'Brian et al. (2007), Wilkinson et al. (2007b,a), Cary et al. (2007), Chang et al. (2007)
A. flavus	39.9	oligo	Kim et al. (2008)
A. flavus	6.0	cDNA	O'Brian et al. (2003), Price et al. (2005)

[a] This array is available from the Pathogen Functional Genomics Resource Center (PFGRC)
[b] This is discussed in detail in chapters 5 and 6
[c] This array is proprietary of DSM, the Netherlands
[d] These two arrays are designed from two different sets of predicted genes
[e] This array was presented and defined in this study
[f] No publication was found using this recently designed array
[g] This array was designed from the *A. flavus* genome sequence, but has also been used for studies of *A. parasiticus*

tion of pathogenicity, spatial differentiation in the hyphae and direction of metabolic engineering using association analysis.

Functional genomics using microarrays

With the increasing number of genomes of Aspergilli being sequenced and published, the number of potential targets for study is increasing rapidly. However, the speed with which new sequence is generated and the relatively smaller community for genetics in Aspergilli compared to yeast makes high-quality annotation for all of the genes hard to come by.

Automatic annotation is being improved as discussed in chapter 7, but still manual curation is needed for the less studied genes. One approach is using transcriptomics as done for *A. nidulans* in the studies by Sims et al. (2004a,b), who presented two case-studies with slightly different approaches. One study (Sims et al., 2004a), is elucidation of the malate dehydrogenase isoenzymes and the other (Sims et al., 2004b) concerns itself with examining 20 secretion-related genes. However, the approaches could be used for any group of genes of interest with some *a priori* knowledge of the

regulation in the examined organism or a related species.

For the identification and examination of malate dehydrogenases, the first three possible targets were found by using the three *Saccharomyces cerevisiae MDH* genes as "*in silico* probes" and comparing these to the *A. nidulans* genome using blastn. This identified three regions in the *A. nidulans* genome with sequence identity to the corresponding yeast genes. By translating the coding regions of the *A. nidulans* sequence and using hierarchical clustering, it was found that the three *A. nidulans* sequences each paired with a distinct yeast malate dehydrogenase. This functional assignment was confirmed by examining the regulation of the three *A. nidulans* genes, and it was indeed found that the genes behaved according to the functional prediction in a glucose-shift experiment.

Another study by Sims et al. (2004b) used 20 known genes from *A. niger* related to the secretory pathway to identify homologous sequences in *A. nidulans*. The putative exons of these sequences were examined using a custom DNA microarray and found to be regulated on a transcriptional level in a manner mirroring that of the behavior in *A. niger*. Additionally, hypothetical orthologues of the endoplasmatic reticulum (ER) chaperone were found to be up-regulated, which supported the functional assignment.

A number of studies have used a combination of bioinformatics tools such as protein family predictions or sequence homology combined with expression profiling to annotate genes encoding carbohydrate-active enzymes in *A. niger*. A study of Martens-Uzunova et al. (2006) identified glycoside hydrolase of family 28 (pectinolytic functions), and used expression profiling to provide functional assignment to 12 previously undescribed genes. A similar method was used by Yuan et al. (2008b) to examine α-glucan acting enzymes. In the work of Yuan et al. (2008a), putative transcription factors located near inulinolytic genes in the genome sequence were deleted in separate mutant strains, and one transcriptional activator, influencing growth on inulin (InuR), is characterized. The study also identified a list of genes putatively induced by InuR. The work of chapter 9 examines all of the genes coding for carbohydrate-active enzymes predicted in the sequence of *A. niger* ATCC 1015.

Examining regulation of carbon metabolism

Knowledge of the regulation of the central metabolism is useful for understanding the potential for improved product formation or examination of carbon repression mechanisms. Several applications of microarrays are studying this type of regulation in Aspergilli.

Maeda et al. (2004) performed a comparative study in *A. oryzae* with a special emphasis on the excreted hydrolytic enzymes. An EST library of $>$ 16,000 sequences was prepared from mRNA from mycelia grown under several culture conditions, including glucose-rich and carbon-deprived medium. In this case, there were approximately 6000 non-redundant sequences. Of these, 2070 highly expressed sequences were used for the construction of cDNA microarrays. By comparing the expression profiles of cultures grown on different media, it was found that the transcription of genes encoding hydrolytic enzymes was greatest on complex wheat-bran medium. By examining the transcription levels for genes that encode enzymes of the genes of the Embden-Meyerhoff-Parnas (EMP) pathway and the tri-carboxylic acid (TCA) cycle, it was found that both of the pathways are active when grown on glucose.

The use of EST-libraries is a very useful alternative to the genome sequence when that is not available. Another use of the EST library can be to make new functional assignments, analogous to the studies by Sims et al. (2004a,b) described above.

David et al. (2006) used oligo-nucleotide arrays covering the majority of the identified genes in the *A. nidulans* genome. Their analysis also involved a reconstruction of the metabolic network from genomic sequences, and in this process they annotated more than 500 metabolic genes. Through combination of the reconstructed metabolic network and transcription profiling during growth on three different carbon sources (glucose, glycerol and ethanol), they identified co-regulated metabolic genes and mapped the operation of the metabolic network during growth

on these three carbon sources.

The work of Mogensen et al. (2006) used a custom array for genes in *A. nidulans* to study carbon catabolite repression at the level of transcription by comparing a *creA* deletion strain to a wild type grown on either glucose or ethanol. The study found a number of indirect effects of the *creA* deletion, and showed that ethanol, which has been thought to be a non-repressing carbon source, still induces some of the carbon catabolite repression components.

Transcription-regulated pathogenicity

A large effort has been put into examining pathogenicity of Aspergilli, mainly by comparing aflatoxin-producing strains of *A. flavus* and *A. parasiticus* as well as general studies on virulence and morphology in *A. fumigatus*. One of the first examples of this, is the work of O'Brian et al. (2003), where an *A. flavus* cDNA clone library was used to identify new genes from *A. parasiticus* associated with aflatoxin production. A very similar approach is used by Price et al. (2005), but in this case the clone library was applied to identify a gene which decreases aflatoxin production when over-expressed.

The functions of a number of regulators of secondary metabolism have been examined using comparisons between expression indices in the wild type and the deletion strain. AflR, the regulator of the aflatoxin biosynthetic cluster, was examined in this fashion in *A. parasiticus* grown under conditions favoring aflatoxin production, thereby identifying genes not in the gene cluster that were influenced by the deletion of the gene (Price et al., 2006). Other studies include deletion of the *A. fumigatus* virulence and morphology-regulating factor StuA (Sheppard et al., 2005), the global regulator of secondary metabolism LaeA in *A. fumigatus* (Perrin et al., 2007), and the toxin regulator VeA in *A. flavus* and *A. parasiticus* (Cary et al., 2007).

The transcriptional response to the exposure to antifungal compounds or suppressors of virulence has also been the target of study. da Silva Ferreira et al. (2006) performed time-course transcriptome analysis of *A. fumigatus* exposed to the antifungal drug voriconazole to study the development of drug resistance. Meyer et al. (2007) studied drug resistance through the transcriptional response of *A. niger* to sublethal doses of the antifungal drugs caspofungin and fenpropimorph, inhibitors of glucan synthesis and ergosterol synthesis, respectively. The main result of this study was that the cell compensates for the inhibited processes by up-regulation of genes with similar function and cell-wall strengthening properties. A very interesting result is that of Kim et al. (2008), where transcription analysis of cultures grown in the presence of the antioxidant caffeic acid showed that it decreases both aflatoxin production and the transcription level of the 29 genes of the aflatoxin gene cluster, suggesting that aflatoxin production is triggered by a response to oxidative stress.

A reciprocal approach to understanding aflatoxin production is that of Chang et al. (2007), where instead of examining drug resistance, *A. flavus* loss-of-aflatoxin production mutants were cultured and analyzed. This confirmed the involvement of many of the genes detected in the studies above.

Spatial differentiation

An often overlooked phenomenon in the study of fungal metabolism is differentiation in the mycelium. More often than not, the cells grow as a multicellular organism with a distinct difference between hyphal tip and the center of a pellet or the base of a substratum, as well as a difference of age between center and rim of the fungal colony.

A transcript profiling study of hyphal differentiation in *A. oryzae* was done by Masai et al. (2006). By separating the mycelium from the solid substrate with a cellulose acetate membrane and inoculation at one end of a square agar plate, the mycelium was made to grow in uni-directionally on top of the membrane. This technique allowed expression analysis of three distinct sections of the colony, namely the base, the white mycelium and the hyphal tips.

An even more sophisticated method is the ring-plate system presented by Levin et al. (2007b) that allows the division of a agar-plate-grown culture into five concentric circles. Transcriptome analysis of these circles allows tran-

scription profiling across a fungal colony in *A. niger* (Levin et al., 2007a). This study showed clear spatial differentiation in areas of metabolism such as nitrate assimilation, secretion and proteases, as well as distinct differences in expression patterns on maltose versus xylose cultivations.

EST mining

An example of the use of functional annotation based on the use of an EST library is presented by Chigira et al. (2002). Initially, two candidate chitin synthases were found in a database of *A. oryzae* ESTs and cloned from the available sequence. The genes were sequenced and characterized, and one was selected for further analysis. Afterwards, the transcription levels of the selected chitinase gene were compared to the levels of other chitin synthases using microarrays.

In the work of Ray et al. (2004), two *A. nidulans* EST libraries (one from glucose growth and one from growth on polysaccharide) were compared to find genes induced on the polysaccharides using a method called negative subtraction hybridization allowing the identification of unique ESTs in one library compared to another library. These results were validated using a microarray, thus presenting both a new method and a list of induced genes.

Association analysis: Directing metabolic engineering

Perhaps one of the best examples of the use of transcriptomics in Aspergilli that is also applicable for metabolic engineering was presented by Askenazi et al. (2003). The authors developed a method, referred to as association analysis, which has the potential to decode the relationship between gene expression and metabolite levels. The method was applied to lovastatin and (+)-geodin production in *A. terreus*.

Initially, 21 strains with different yields of lovastatin and (+)-geodin were constructed and their gene expression was examined on microarrays containing approximately 21,000 random genetic elements with an average length of 2 kb. Additionally, metabolite-levels were determined using high performance liquid chromatography (HPLC) and mass spectrometry (MS). Association analysis was performed on the combined metabolic and transcriptional data. By reducing the complexity of the transcription data to up-, down- or no significant regulation for the transcription data, and decrease/increase in level for the metabolite data, an algorithm was employed to determine which genetic elements were significantly associated with metabolite production.

The association analysis was able to successfully identify the lovastatin biosynthetic cluster as being associated with lovastatin production. Additionally, it identified several previously unknown genetic elements correlated with geodin production, including the polyketide synthase. In addition to functional assignment, association analysis also provides information on the regulation of central pathways relative to production of secondary metabolites.

In the context of metabolic engineering, association analysis is a valuable tool. In addition to the discovery of new targets to engineer, several other uses are proposed and tried. First, the information on regulation of the central pathways gives pointers to which regulatory elements it could be profitable to un-couple. Second, if the analysis is performed with the yield of an unwanted by-product, one could find targets for elimination, and thus potentially improve yields of the wanted compound, and make downstream processing less cumbersome. Third, as demonstrated by Askenazi et al. (2003), promoters from genes correlated with metabolite yields can be used for making efficient reporter systems.

Identification of secondary metabolite clusters

The study of Bok et al. (2006) examined the potential of *A. nidulans* to produce novel secondary metabolites, but the method can be applied to any filamentous fungus with a sequenced genome. Secondary metabolites differ from other metabolites in filamentous fungi on the genomic level in that the genes of the biosynthetic pathway are often arranged in clusters. By examining the up- or down-regulation as a function of the position of the genome, clus-

ters that are co-regulated can be found. Bok et al. (2006) used this to find the cluster for the biosynthesis of a novel metabolite, terrequinone A. See also chapter 7 for an example of identification of active secondary metabolite clusters in *A. niger*.

2.1.3 Proteomics

A recent review of proteomics in filamentous fungi uses a definition of the proteome to be the "global set of proteins expressed in a cell at a given time and biological state" (Kim et al., 2007b). While the presence of a genome sequence allows the identification of a protein from information on the amino acid sequence, the limitation in proteomics is often the purification, separation, detection and quantification of the individual proteins. A number of general methods mainly developed in *Escherichia coli* and *S. cerevisiae* have been published for this, including, but not limited to, isotope-coded affinity tags (Gygi et al., 1999), protein arrays (Zhu et al., 2001), two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) combined with MS of excised proteins (Bader and Hogue, 2002), and yeast two-hybrid systems (Auerbach et al., 2002). However, a direct adaptation of the protocols from yeast is not possible due to more sturdy cell walls, making the cell-lysing step of the preparation limiting in filamentous fungi (Kniemeyer et al., 2006). Additionally, heavily glycosylated proteins, found especially in the extracellular fraction, often have varying masses and are difficult to separate clearly as the isoelectric point can vary with the glycosylation. Method-development in proteomics of Aspergilli is being actively pursued, and the review by Kim et al. (2007b) refers to four studies presenting methods for sample preparation in relation to Aspergilli. Even so, all but two of the *Aspergillus* studies presented here, were done using 2D-PAGE for separation and MS for identification.

The limitation in the experimental procedures, perhaps combined with the relative ease of transcriptomics, means that the number of studies on *Aspergillus* proteomics is rather low compared to transcriptomics. Often, what is identified is a small percentage of the proteome or a so-called subproteome, a more or less defined subset of the proteome (Cordwell et al., 2000). Of special relevance to filamentous fungi, both in the context of industrial and medical applications, is the intracellular and extracellular subsets as well as proteins present in the cell wall and/or membrane. This section will make an overview of the proteome studies in Aspergilli in a roughly chronological order, with a particular focus on the progression in the number of separated and identified proteins as well as the examined fractions. A timeline of the studies showing the statistics of separation and identification can be found in Figure 2.1.

Perhaps the first proteome study in Aspergilli is that of Bruneau et al. (2001), where the subproteome of proteins glycosylphosphatidylinositol (GPI)-anchored to the cell wall of *A. fumigatus* is examined. Using a sophisticated combination of enzymatic cleavage of the anchor, polyclonal antibodies and 2D-PAGE/MS, this group of morphogenesis proteins was studied prior to the release of an *A. fumigatus* genome sequence by comparison to the *S. cerevisiae* genome.

Following that is the work of Melin et al. (2002), which must be the first comparative proteomics study in Aspergilli. Here, more than 200 peptide spots from *A. nidulans* were separated and at least 20 of these were found to be differentially regulated in a comparison of cultures treated with the antibiotic concanamycin A to a reference culture. Five of these were identified.

The work of Medina et al. (2004) examined enzymes secreted from *A. flavus* when grown on the flavonoid rutin or potato dextrose. The method obtained separation of more than 110 peptides, and identified 15 rutin-induced proteins and 7 non-induced proteins. A continuation of this study (Medina et al., 2005), expanded the growth conditions to include a glucose medium and refined the separation and detection methods to identify 51 secreted proteins.

With a special focus on the drug resistance response, Ström et al. (2005) studied the effect of antifungal compounds secreted from *Lactobacillus plantarum* on *A. nidulans* by comparing to a control cultivation. A systemic response could be observed on the gels, and two differentially regulated genes were identified.

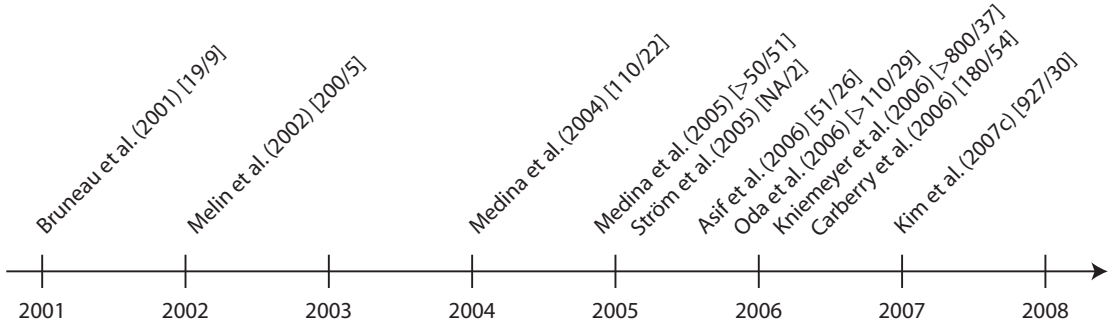

Figure 2.1: Timeline of proteomics studies in *Aspergillus* species. Numbers in sharp brackets are number of separated peptides/number of identified peptides. "NA" denotes that the information was not available.

Asif et al. (2006) examined the subproteome of the *A. fumigatus* conidial surface in search of potential antigens. Using 2D-PAGE/MS followed by liquid chromatography (LC) and tandem MS/MS, 26 proteins were identified, among these a known allergen, thus proving the validity of the method.

A study of protein secretion in *A. oryzae* by comparative proteomics of extracellular proteins from solid-state and submerged cultures was conducted by Oda et al. (2006). Eighty-five peptide spots from the solid-state culture and 110 spots from the submerged culture were analyzed and 29 of them identified. A similar analysis of the subproteome of the cell-wall bound fraction allowed a mapping of the secretion/retention pattern of the identified proteins, indicating that some proteins were expressed but retained in the cell wall in one culture while being excreted in the other.

Kniemeyer et al. (2006) evaluated a number of different methods of sample preparation for 2D-PAGE/MS and the best resulted in separation of more than 800 peptides from the intracellular fraction of proteins from *A. fumigatus*. The best method was used to examine the protein fractions detectable in cultures grown on glucose or ethanol, where 37 differentially regulated proteins were identified.

In a study of glutathione transferases from *A. fumigatus*, Carberry et al. (2006) examined these potential mediators of resistance to oxidative stress and antifungal drugs or xenobiotics. In a proteome-survey, 180 peptides were separated and 54 intracellular proteins were identified. Using chromatography, the authors also performed a study of the subproteome consisting of glutathione binding proteins. From this, 10 proteins were separated and four of them identified followed by the characterization of one of the proteins.

The latest general proteome study and the one with the highest resolution is that of Kim et al. (2007c), where osmoadaptation in *A. nidulans* was investigated by comparative proteomics on a normal liquid culture medium versus growth in the same medium with 0.6 M KCl. 927 distinct protein spots were identified and 90 of these were determined to be differentially expressed, of which 30 were identified.

In a very applied and focused example of the potentials of *Aspergillus* proteomics, Kim et al. (2007a) used a novel combination of 2D-PAGE of secreted enzymes from *A. fumigatus* with an in-gel assay for β-glucanase activity to identify expressed β-glucanases. The detected β-glucanases were identified using MS, and a novel heat-resistant β-glucanase was characterized.

While it is clear from the above studies that the coverage and efficiency of *Aspergillus* proteomics are still in its infancy, the potential of the technique is evident. Especially the studies taking advantage of the protein separation, such as that of Oda et al. (2006) or Kim et al. (2007a), are producing results that would be difficult to

obtain using other techniques.

2.1.4 Metabolomics

The study of the full set of metabolites in the cell (metabolomics) is, compared to genomics, transcriptomics, and proteomics, a more complex task due to the large variation in the physical and chemical properties of the metabolites. Excluding sample-preparation, which can require several fractions and/or derivatization such as the method presented by Villas-Boas et al. (2003), combinations of analytical methods are required to separate and identify the metabolites. This has lead to the development of a number of high-throughput tandem methods for quantitative analysis including gas chromatography-mass spectrometry (GC-MS), gas chromatography-time-of-flight mass spectrometry (GC-TOF), and liquid chromatography-mass spectrometry (LC-MS) (Villas-Boas et al., 2005), as well as direct infusion mass spectrometry (diMS), a metabolome profiling technique developed specifically for fungi (Smedsgaard and Nielsen, 2005). While the potential is thus present (Fernie et al., 2004), very few research papers have been published doing large-scale quantitative studies in Aspergilli. One such is the work of Askenazi et al. (2003) discussed in section 2.1.2, where the combined analysis of metabolome and transcriptome were employed to improve the yield of lovastatin and identify new genes.

Another recent example, and perhaps the best example of metabolomics in an *Aspergillus* species, is the work of Kouskoumvekaki et al. (2008), where metabolic profiles based on more than 450 metabolites from *A. nidulans* were used to identify seven biomarkers indicative of the genotype of the strain. This method can identify mutants producing the model polyketide 6-methylsalicylic acid in high-yields.

2.1.5 Modeling

Generally, two methodologies of systems-wide modeling of metabolism have been applied in microbial systems (Nielsen, 1998). One is metabolic flux analysis (MFA) or flux balance analysis (FBA) characterized by the calculation of carbon fluxes using a list of biochemical reactions available to the cell (a stoichiometric model) and applying mass balances for each metabolite. Typically, carbon fluxes across the cell membrane are estimated by measuring extracellular concentrations and biomass and used to calculate the fluxes inside the cell. Stoichiometric models for the central metabolism and full genome-scale of *A. niger* (David et al. (2003), Melzer et al. (2007), Andersen et al. (2008a), and chapter 3) and a genome scale model for *A. nidulans* (David et al., 2006) have been published previously, and a genome-scale model for *A. oryzae* is currently in review (Vongsangnak *et al*, personal communications).

The other main modeling approach is kinetic modeling. One framework for this is metabolic control analysis (MCA). This approach focuses on modeling the flexibility of the enzyme activities in a pathway by setting up two differential equations for each biochemical reaction in the model, called elasticity coefficients and flux control coefficients (FCCs) (Fell, 1992). The first expresses the correlation of reaction rate to metabolite concentrations and the FCC is an expression of the sensitivity of the flux towards the enzyme activities in the metabolic network. In order to derive the elasticity coefficients and the FCCs, it is necessary to either titrate the enzyme level inside the cell or to set up a kinetic model for the individual enzymatic reactions in the metabolic network under study. The latter requires extensive information on the kinetics of the individual enzymes as well as solid data on the intracellular metabolite levels, and is therefore laborious to obtain. To circumvent this problem, it has been proposed to use generalized kinetic expression, the so-called S-system, where the kinetics of each reaction in the network are described as a power-law function of all the metabolites in the network (Voit, 2005).

Stoichiometric modeling

The use of FBA has several useful properties for metabolic engineering. The main strength is the power to elucidate the distribution of carbon fluxes and identifying key branching points in the cellular pathways, which improves the selection of targets for engineering. One also

has the possibility of examining whether the insertion of new enzymes or entire pathways has the potential to improve the yield. Yet another use is the calculation of the maximum theoretical yields (Nielsen, 1998), allowing estimation of the commercial relevance of production of a given metabolite/protein in the modelled organism. Price et al. (2004) describe a toolbox available for the analysis of stoichiometric models of microbial cells.

Several stoichiometric models exist for *A. niger*. An early model for *A. niger* central carbon metabolism was presented by David et al. (2003). In this case, the model was applied to search for strategies to improve succinate production. When testing all combinations of two gene deletions, it was found that a fruitful strategy might be a deletion of ATP:citrate oxaloacetate-lyase and pyruvate decarboxylase giving a yield of at least 1.12 mol succinate per mol glucose. A smaller model of *A. niger* metabolism has been presented by Melzer et al. (2007) based on the model of David et al. (2003) and other information, and was used to predict metabolic fluxes through pathways of central metabolism in cultivations on two different media and at varying levels of ambient pH. A comprehensive model of *A. niger* metabolism and the validation and analysis of it is presented in chapter 3.

For *A. nidulans*, a stoichiometric model has been developed by David et al., and applied for studies in the publications of David et al. (2006) and David et al. (2008). The model was used to improve the functional annotation of 472 genes as well as aiding in the interpretation of transcriptome data.

Kinetic modeling

Torres et al. have addressed the kinetic modeling of glucose metabolism in *A. niger* in several articles (Torres et al., 1993, Torres, 1994a,b, Torres et al., 1998). In the publications of Torres et al. (1993) and Torres (1994a), the model for glucose metabolism is presented and tested for stability. Torres (1994b) analyzed the system, and came to the conclusion that an up-regulation of the hexokinase transporter would be beneficial to the citrate production. A further analysis with newer algorithms (a variation of MCA) in 1998 (Torres et al., 1998) found the optimal production of citrate while still holding the metabolite pools approximately constant. However, this solution suggested that the simultaneous modulation of seven or more enzymes are required to optimize citrate production.

The model was further improved with an increased complexity and used in the study by Alvarez-Vasquez et al. (2000). This model represents the main pathways involved in citric acid production including the mitochondrial reactions, which were not included in the study by Torres et al. (1998). When applied to the optimization of citric acid production, it was found that the maximum potential was not yet reached, and that the rate of citrate production could be increased by a factor of 3- to 50-fold, but the further increase would require the modification of a minimum of 13 enzymes. The implications of this result is discussed in section 2.2.1.

Another dynamic pathway modeling in *A. niger* was performed by de Groot et al. (2005) where MCA was employed to examine the potential to grow on L-arabinose. The goal was to find targets for metabolic engineering so that organic waste may be used for production processes involving *A. niger*. By examining the FCC's it was found that the first three enzymes of the pathway, L-arabinose reductase, L-arabitol dehydrogenase and L-xylulose dehydrogenase would be the most profitable targets.

2.2 Examples of metabolic engineering of Aspergilli

While the definitions of metabolic engineering, such as the one by Bailey (1991) mentioned in the introduction to this chapter, do not necessitate the application to commercial processes, it is indeed mostly applied in this context, due to the philosophy of improving productivity. For this reason, a review of metabolic engineering is also a review of the commercial products of the Aspergilli. Four major groups of commercial products from members of the *Aspergillus* genus have been targets of metabolic engineering:

Citric acid: Originally, production of citric acid was initiated due to a shortage of Italian lemons during the first world war, and remains in use as a substitute for lemons. As an acidifier and flavoring agent (E330 in the European system for food additives), citric acid is added to food, candy and soft drinks. Since citric acid is a tri-carboxylic acid (pK_{a1-3}: 3.15, 4.77, 6.40) and an excellent buffer, it is widely used in household cleaners. The make-up of the molecule makes it capable of chelating metals (from calcium to heavy metals), which is a useful property in detergents (Karaffa et al., 2001, Karaffa and Kubicek, 2003). Additionally, it finds use in the biotechnology and pharmaceutical industry for the cleaning of stainless steel pipes, where it is considered an environmentally friendly alternative to inorganic acids. With its versatility, the annual world market for citric acid reached $1.2 billion in 2002. By far the majority of this market is covered by fermentation with *A. niger*.

Extracellular enzymes: The use of enzymes as biocatalysts in the industry are many and diverse. A few examples are for food products, in cosmetics and care products, in textile industry and as detergents. The world market for industrial enzymes was thus close to 3.1 billion US dollars in 2007 (Novozymes, 2008). Due to the fact that filamentous fungi have a large potential for production of secreted proteins, and can be cultivated in submerged cultures, enzymes produced by filamentous fungi amounted to as much as half the market in 2001 (Yoder and Lehmbeck, 2004). Numbers for 2007 suggests that the percentage still holds true (Novozymes, 2008). The main targets for metabolic engineering have been α-amylase and gluco-amylase from *A. niger* and *A. oryzae*.

Recombinant proteins: Several fungal hosts not of the *Aspergillus* genus such as *Trichoderma reesei* (Penttilä, 1998, Hjort, 2003, Nevalainen et al., 2005) and *Fusarium venetatum* (Yoder and Lehmbeck, 2004) have seen use for the production of recombinant protein. However, the main workhorses in the field has traditionally been *A. niger* and *A. oryzae*, as processes involving these organisms have been classified as Generally Regarded As Safe (GRAS) by the FDA for a long time (Hjort, 2003). Some examples of heterologous proteins expressed in these two hosts are *Candida antarctica* lipase B (Conelly and Brody, 2004), *Scytalidium thermophilum* catalase (Conelly and Brody, 2004), *Trametes versicolor* laccase (Valkonen et al., 2003), bovine preprochymosin (Valkonen et al., 2003), *A. niger* α-galactosidase (Knap et al., 1994), *A. oryzae* stereo-selective esterase, chymosin (Hjort, 2003) and others, but the actual number of products far increase that and the potential is virtually endless. A review by Yoder and Lehmbeck (2004) provides an extensive list of heterologous proteins and hosts. Metabolic engineering of strains for protein production allows for the production of proteins from potentially any organism.

Biopharmaceuticals: While the list of native biopharmaceuticals from the Aspergilli is rather short, the group of secondary metabolites named statins, particularly lovastatin (also known as mevinolin) from *A. terreus* has attracted attention based on its abilities as a potent cholesterol-lowering agent. The commercial production of lovastatin has been carried out since 1980 (Alberts et al., 1980, Manzoni and Rollini, 2002), and has been been sold in clinical formulations by Merck & Co as Mevacor.

The metabolic engineering effort in each of these four groups of products will be covered in the following sections.

2.2.1 Citric acid production by *A. niger*

Traditionally, the strain improvement for the production of citric acid has been done by classical methods, e.g. mutagenesis and screening (Hjort, 2003), leading to concentrations of citrate in the fermentation broth of >100 g/L (Netik et al., 1997). Modern production strains can yield up to 95 % citrate from sucrose in controlled fermentations (Karaffa and Kubicek, 2003). This high yield leaves little room for improvement by metabolic engineering, however, several investigations have been performed in research strains, and generated ex-

tracellular concentrations of citrate as high as 55 g/L (Ruijter et al., 1998).

The early attempts at metabolic engineering of citric acid production is presented in an excellent review by Ruijter et al. (1998) where several general strategies are presented. One such strategy is decreased by-product formation.

A. niger is, as other Aspergilli, characterized by producing a number of organic acids and polyols (Witteveen et al., 1993). Among these, gluconic acid and oxalic acid are the main problems in production of protein products. Gluconic acid is produced outside the cell by glucose oxidase, and reduces the carbon flow towards citrate (Witteveen et al., 1992, Ruijter et al., 1998). The production of oxalic acid is a drain on the available carbon, but oxalic acid also precipitates with calcium-ions, thus complicating the purification of citrate in the down-stream processing (Oxalic acid is toxic and not wanted in food grade chemicals). A glucose oxidase deficient *A. niger* strain has been constructed by Witteveen et al. (1990b), but whether this increased the citrate yield was not measured.

The use of a production strain without oxaloacetate hydrolase, and thus without the capability of producing oxalic acid has been patented by Hjort and Pedersen (2000) based on the characterization of Pedersen et al. (2000c). The elimination of oxaloacetate hydrolase is also desirable in the production of polypeptides as discussed in section 2.2.4.

Torres et al. (1993) has used sensitivity analysis of the citrate system to show that there are at least three control steps in the production of citric acid: (1) hexose uptake and/or phosphorylation, (2) mitochondrial citrate export and (3) export through the cytoplasmic membrane.

Initial efforts to understand the hexose-phosphorylation and uptake in the context of citrate production came from studies by Schreferl-Kunar et al. (1989), where mutagenised strains were screened for enhanced growth and increased production of citrate. Mutants with more than a 20 % increase in citrate production were found to have faster sucrose uptake and the activities of hexokinase and phosphofructokinase were increased. Torres (1994a,b), and Torres et al. (1998) examined the entire glucolysis by kinetic modeling. In this, it was demonstrated that the levels of seven to ten enzymes have to be regulated to maximize the flux through glycolysis, including the hexokinase/transportsystem. Additionally, as the authors recognize, this may be difficult to achieve due to the interconnectivity of the regulation of the pathway with other parts of the metabolism. Some of the enzymes suggested modulated by Torres et al. (1998) was overexpressed in a study by Ruijter and Visser (1997), where the levels of phosphofructokinase and pyruvate kinase levels was increased. However, as Torres et al. (1998) suggests, these modifications alone did not significantly improve the citrate production.

The mitochondrial part of the citrate system consists at a minimum of the pyruvate importer, pyruvate dehydrogenase, the citrate synthase and the citrate-malate anti-porter (see Figure 2.2). Although there has not been published any direct modulation of the pyruvate importer or pyruvate dehydrogenase, the citrate synthase has been 11-fold overexpressed by Ruijter et al. (2000). However, as Ratledge (2000) points out, there is a large capacity of the mitochondrial citrate synthase, and therefore overexpression of citrate synthase has no effect on the citrate production, as was also found by Ruijter et al. (2000). The malate-citrate anti-porter has not been studied directly in *A. niger*.

The citrate export system has been examined by Netik et al. (1997), and found to be dependent on the absence of manganese and is likely to be symported with protons. A recent study by Burgstaller (2006) found that passive transport would be sufficient at extracellular pH as low as 3. However, both studies agree that the citrate gradient over the cytoplasmic membrane is the limiting factor. Based observations and modeling results of this type, and studies of the mitochondrial citrate transporter, where Sandor et al. (1994) showed that the concentrations of di-carboxylic acids influenced the transporter, de Jongh and Nielsen (2008) presented an application of metabolic engineering of *A. niger*. In this study, combinations of several genes of the reductive part of the TCA from *S. cerevisiae* and *Rhizopus oryzae* were inserted in *A. niger*, with a maximum yield of 0.9 g citrate per g of glucose.

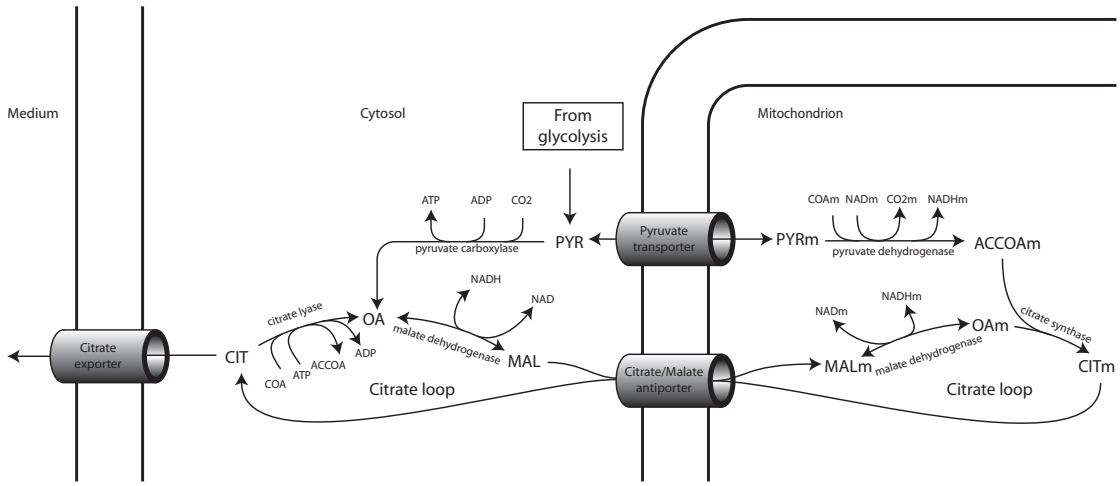

Figure 2.2: The citrate system in *A. niger*

The application of this study has been patented by Nielsen and de Jongh (2007).

Discussion

Metabolic engineering of the citrate production system in *A. niger*, as described above, has been attempted by several researchers, and with increased production of citrate as a result in several of these studies. However, as studies by Torres et al have shown, the native enzymes of the glycolytic pathway are difficult to engineer, and that a large number of manipulations are necessary to obtain high yields. Additionally, apart from the patent of Nielsen and de Jongh (2007), no patents exist for improving the citrate production of fungal strains by metabolic engineering. One might therefore assume that strain improvement to the largest extent, until now has been performed by classical methods. The study by de Jongh and Nielsen (2008) shows, however, that the insertion of heterologous genes may circumvent the tight regulation of the system with relatively few manipulations, and give yields competitive with those of classical strain improvement techniques.

2.2.2 Glucoamylase production in *A. niger* and *A. oryzae*

Glucoamylase (Enzyme Commission (EC) number 3.2.1.3) is used in the food industry for converting starch into glucose syrup. This process was previously performed by chemical means — acidic hydrolysis using hydrochloric acid — which gave several by-products and salt formation when the reaction mixture was neutralized and concentrated. The conversion to a biotechnological process using glucoamylase made the process less costly and gave a higher quality of the product. This was one of the first large scale enzymatic processes, and even today the starch industry uses by volume the largest amounts of enzymes (Hjort, 2003). The main fungal workhorses for this production are *A. niger* and *A. oryzae*.

The optimization of glucoamylase production can be divided in to two main categories: Effect of gene dosage and morphology engineering. The first type deals mainly in increasing the production of amylase, whereas the other enhances the excretion of the protein.

Effect of gene dosage

A simple and effective method of improving the production of glucoamylase by *A. niger* was performed by Wallis et al. (1999) by inserting 80 extra copies of the gene into the genome. The enhanced strain secreted five to eight-fold more protein than the parent strain. An interesting observation made was that the glycosylation of the produced protein was similar to the wild

type due to an up-regulation of glycosylation enzymes.

Maiyuran et al. (2005) presents the regulation of expression of genes or clusters thereof by using mRNA silencing. The two strategies presented are transcription of the full reverse complement of the gene to be silenced, and transcription of small interfering RNAs, possibly targeted towards clusters of genes with homology. The test systems were glucoamylase activity in *A. niger* and *A. oryzae*. Both were transformed with a vector containing a suitable promoter and an inverted repeat DNA-construct, when transcribed, produced a hairpin double stranded RNA matching the mRNA of the glucoamylase. For *A. niger*, the glucoamylase activity was reduced to 1 %.

Morphological engineering

Some studies of the anatomy of fungal cell indicates that protein secretion is highly localized to the hyphal tip (Peberdy, 1994). This has increased commercial interest in studies of the morphology, and several methods have been presented to improve the protein secretion by changing the morphology of the fungus. Often, the production of glucoamylase has been used as a model system.

Dunn-Coleman et al. (2000) presents the observation that certain mutations involved in the hyphal branching regulation can increase the production of glucoamylase. This line of research was continued by the same group of people in the patent of Pollerman and Memmott (2005), which describes the improvement of protein production by introducing a mutation in the hyphal branching regulator HbrA. The mutation induces hyper-branching when grown at 42°C. In a patented method for improving protein secretion, Akin et al. (2002) present a truncation of the *cotA* gene that gives a compact morphology.

2.2.3 α-amylase production in *A. niger* and *A. oryzae*

Another enzyme important for the large starch processing industry is α-amylase (EC 3.2.1.1), produced by *A. niger* and *A. oryzae*. This enzyme has been subject to some metabolic engineering leading to the patenting of hybrids and variants of the molecule that have improved abilities in starch-processing. Additionally, morphology engineering has been performed for the improvement of the α-amylase production.

Enzymatic engineering

Svendsen et al. (2005) patented a number of variants of fungal α-amylase constructed using 3D-modeling of the protein. Spatial examination of the make-up of the enzyme allowed for the engineering of changes in the catalytic site. The method was applied on α-amylase from both *A. niger* and *A. oryzae*, and in both cases the variants exhibited increased exo-activity on a starch substrate.

The work by Taira et al. (2005) patented a hybrid polypeptide for starch processing. The polypeptide is a three-part construct composed of a catalytic module from α-amylase, a linker sequence and a carbohydrate-binding domain (CBD) (more specifically a starch binding domain in most applications). Different combinations of catalytic unit, linker and CBD from several Aspergilli were presented and screened for activity.

Morphological engineering

Although the improvement of morphology previously has been done mostly by mutagenesis as patented by Shuster and Royer (1997), Müller et al. (2002) present a targeted approach to manipulating the morphology of *A. oryzae*. Chitin synthase B and chitin synthesis myosin A were disrupted and the result was an increased branching of the mycelium. However, this did not increase the production of α-amylase production, but the pelleting of the mycelium was decreased, which resulted in a decrease in the broth viscosity — a desirable property for large scale fermentations.

2.2.4 Heterologous protein production in *A. niger* and *A. oryzae*

When optimizing the production of heterologous protein, several general strategies are used, either alone or in combination. One method of

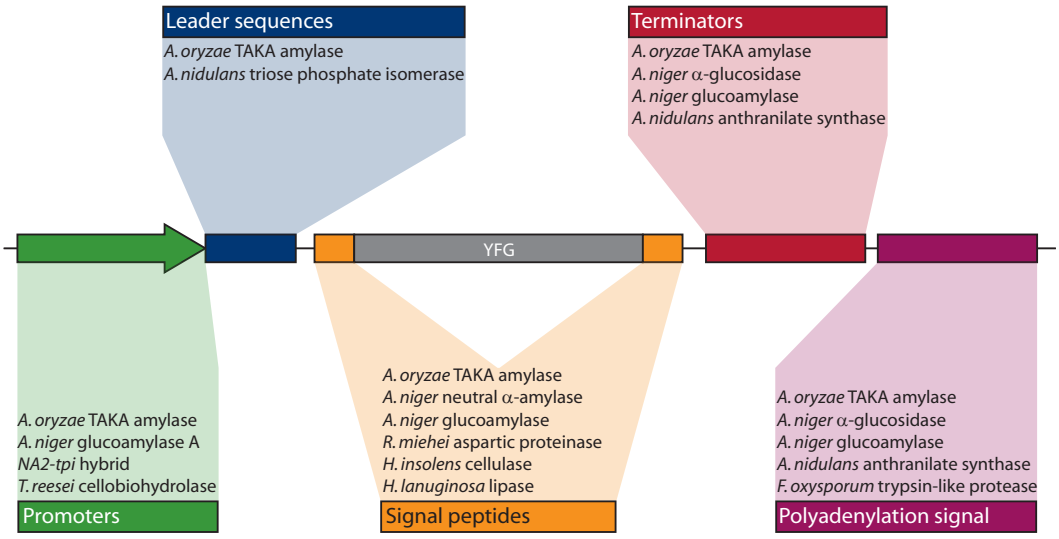

Figure 2.3: Overview of the different cassettes used for heterologous gene production in *A. niger* and *A. oryzae*. Based on information from Conelly and Brody (2004), and Hjort (2000).

improving production is the use of genetic engineering for enhancing promoter activity, copy number, gene properties or other features of the gene itself. Another method is more system-wide changes, where regulators of the gene-expression or competing enzymes are targeted. The final group of strategies is the classical metabolic engineering, where the enzymes of the metabolism is targeted. In several cases, the yield or the production process of proteins benefits from such modifications. This can be due to improved physical/chemical properties of the medium, thus improving down-stream processing, or removal of secreted enzymes competing with the wanted product (by-product formation).

Gene modifications

To ensure high production levels and efficient transport of the protein out of the cell, flanking artificial DNA constructs are used. The up- and down-stream sequences of highly expressed and exported enzymes are recombined with the heterologous gene. The surrounding regions of *A. oryzae* TAKA α-amylase are generally used as a dependable system for high expression (Yoder and Lehmbeck, 2004, Hjort, 2003), but other sequences are in use as well. An overview of the most used sequences in the examined patents is presented in Figure 2.3. Use of these types of DNA cassettes has allowed for yields in the commercial processes higher than 5 g protein/L (Yoder and Lehmbeck, 2004).

The use of synthetic promoters is found in Yaver and Nham (2004), where variations of the *F. venenatum* glucoamylase promoter are patented. These promoters regulates the transcription of fungal genes including glucoamylase and lipase. Specifically, the expression of the gene after the promoter was increased six-fold by adding copies of a domain in the promoter required for high expression. The method is patented for several fungal species, but the most preferred embodiments are with *Aspergillus* or *Fusarium* host cells.

Modified regulators

The targeting of transcription factors can in some cases be a fruitful way of stimulating the production host to produce more protein. One such example is the overexpression of *hacA* by Valkonen et al. (2003) (Patented in Penttila et al. (2001)). HacA has a role as an inducer of the unfolded protein response (UPR) in fungi. This cellular response facilitates for the refolding of unfolded protein, which otherwise would have been degraded by the cell. In the production

of *Trametes versicolor* laccase and bovine prochymosin by *A. niger*, the production was improved 2.9-fold and 7-fold, respectively, by inserting *hacA* with the *A. niger* glucoamylase A (*glaA*) promoter.

Two patents (Hjort et al., 2000, 2001) concerns the activity of the activator of fungal proteases (PrtT). In unmodified cells, a high level of proteases is found in the medium. These degrade the heterologous product, thus lowering the yield. PrtT induces these activities, and is thus a target for deletion. Hjort et al. (2000) patented the use of the activator of fungal proteases (PrtT) in the context of producing polypeptides. The deletion and overexpression of *prtT* are provided as examples. Hjort et al. (2001) patents modifications of transcriptional regulators of proteases to increase the product formation of heterologous proteins. The transcriptional regulator prtT is preferentially obtained from *A. niger*, but disruption of the gene was performed in both *A. niger* and *A. oryzae*. However, none of these patents presents values for the increase in yield, but the technique is used for production of *C. antarctica* lipase B in Conelly and Brody (2004). In this case, protease activity was reduced to a fifth of the wild type level, and product yield increased by 200%.

Deletion of enzymes

A number of enzymes interfere with the production of heterologous protein. One enzyme that deserves special mention is oxaloacetate hydrolase, producing oxalate and acetate. Oxalate is excreted into the medium, and has the ability of precipitating with calcium, which causes difficulties in the downstream processing of the fermentation product. Additionally, this property causes oxalate to be toxic to humans. Finally, the production of oxalate results in loss of carbon in the production organism. Hjort and Pedersen (2000) patented the use of fungal strains with a deletion of the oxaloacetate hydrolase gene, particularly for the production of heterologous polypeptides. Unfortunately, the deletion of the oxaloacetate hydrolase decreases the glucoamylase production by 50% (Pedersen et al., 2000b).

Other strategies includes the deletion of genes coding for by-products, i.e. other secreted enzymes. The patent by Conelly and Brody (2004) provides perhaps the most comprehensive overview of the improvement of production of recombinant protein in *A. niger*. A comprehensive study of the effect of combinations of enzyme deletions on production of *Candida antarctica* lipase B and *Scytalidium thermophilum* catalase is provided. The deleted enzymes and genes include: oxaloacetate hydrolase (*oah*), glucoamylase (*glaA*), acid stable α-amylase (*asa*), *prtT* and neutral α-amylases (*amyA* and *amyB*). Strains with the *prtT* deletion and combinations of enzyme deletions were used to produce the above mentioned lipase and catalase. The yield of *C. antarctica* lipase was improved three-fold over an eight day fermentation mainly due to a protease activity drop to 20%. The *Scytalidium thermophilum* catalase yield increased by 40 % in the best of the mutant strains.

2.2.5 Lovastatin production in *A. terreus*

In the improvement of the production of lovastatin, classical strain improvement e.g. random mutation and screening strategies has been extensively used to obtain over-producing strains (Kumar et al., 2000b, Vinci et al., 1991). Furthermore, process development programs, such as fermentation optimization, medium design and scale-up have been applied to increase the productivity and yield of lovastatin (Bradamante et al., 2002, Casas Lopez et al., 2003, Hajjaj et al., 2001, Kumar et al., 2000a, Lai et al., 2002). An *A. terreus* mutant strain from 2006 produces lovastatin up to 16 g/L, whereas only 30–60 mgL was produced by the initial strain (Matkinen News February 2006; Metkinen Oly, Finland). This hyper-producing process and strain was obtained by using combined (chemical and physical) mutagenesis methods as well as a process development program. During strain development, several efforts were put into investigation and understanding the biosynthetic pathway of lovastatin using nuclear magnetic resonance and mass spectroscopy (Chan et al., 1983, Moore et al., 1985, Yoshizawa et al., 1994). These results revealed that lovastatin is

derived from two distinct polyketide chains, a nonaketide and a diketide, joined through an ester linkage. Recently, the polyketide synthase (PKS) gene involved in lovastatin biosynthesis has been isolated and characterized (Hendrickson et al., 1999). This PKS gene is required for the biosynthesis of the nonaketide backbone of lovastatin and was named *lovB*. Based on the knowledge that genes involved in secondary metabolism are organized in physical clusters on the genome, the entire lovastatin gene cluster was cloned using *lovB* as a probe and characterized (Kennedy et al., 1999). Nine genes (*lovA*–*lovH* and *ivrA*) are assumed to encode polypeptides required for lovastatin biosynthesis (Auclair et al., 2001, Hutchinson et al., 2002, Kennedy et al., 1999). Increasing knowledge of the lovastatin biosynthetic gene cluster has led the way for applying metabolic engineering to the improvement of lovastatin productivity. Consequently, several research projects have focused on improvement of lovastatin production by manipulating the regulatory control. Introducing extra copies of the specific regulatory gene *lovE* into *A. terreus* wide-type strain led to increase the amount of lovastatin by at least two-fold. Some transformants were found to produce five-fold to seven-fold more lovastatin than the wild-type strain. Recently, a novel *Aspergillus* nuclear protein (LaeA), which assumed to act as a global regulator of secondary metabolites in *Aspergillus sp.*, was discovered by complementation of a sterigmatocystin mutant (Bok and Keller, 2004). The role of LaeA was investigated by deletion and overexpression of *laeA* in *A. fumigatus*, *A. nidulans*, and *A. terreus*. Deletion of *laeA* resulted in a decrease in sterigmatocystin, penicillin and lovastatin gene expression. On the contrary, increasing in the transcription of penicillin and lovastatin and subsequent product formation was observed in *laeA* overexpression strains.

Another example by Kennedy et al. (1999) and Hutchinson et al. (2002) is the heterologous expression of the truncated lovastatin gene cluster in non-lovastatin-producing organisms, i.e. *A. nidulans*. Two *A. nidulans* transformants were found to be significantly resistant to lovastatin compared to the reference strain. Furthermore, both transformants were able to produce lovastatin intermediates, monacolin J and monacolin L.

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Chapter 3

Metabolic model integration of the bibliome, genome, metabolome and reactome of *Aspergillus niger*

> "Now the general who wins a battle makes many calculations in his temple ere the battle is fought. The general who loses a battle makes but few calculations beforehand. Thus do many calculations lead to victory, and few calculations to defeat: how much more no calculation at all!"
> *Sun Tzu — The Art of War*

As one may get the impression from chapter 2, it is difficult to think of a filamentous fungus where the metabolic capabilities are of greater interest than *A. niger*. As a widely used industrial workhorse, the commercial applications of *A. niger* range from the high yield production of citric and gluconic acid, through production of a range of industrial enzymes in high titers and the production of heterologous proteins such as chymosin or human interferon (Dunn-Coleman et al., 1991, van Brunt, 1986, Punt et al., 2002, Karaffa and Kubicek, 2003, Singh and Kumar, 2007). With such an impressive diversity of high-yield products, *A. niger* holds the potential to become an even more versatile cell factory platform in the future. The publishing of the genome sequence of *A. niger* CBS 513.88 (Pel et al., 2007), has made it apparent that this fungus holds a genetic diversity, that is a potential trove of new products. Some genomics-based products have already been commercialized (see section 2.1.1). As commented by Cullen (2007), there is now a great potential for increasing the yield of both known and novel products by directed metabolic engineering. However, data-integration on a systemic level is necessary to fully understand and exploit the potential of the metabolism.

In order to increase the understanding of central metabolism in *A. niger*, a number of models and overviews have been presented (Torres, 1994a,b, Röhr and Kubicek, 1981, Pedersen et al., 2000b, Karaffa and Kubicek, 2003, David et al., 2003, Gheshlaghi et al., 2007, Schmidt et al., 1999). While these models describe specific aspects of metabolism well, no model has ever integrated a full genome-scale metabolic network with genomic annotation. A complete and accurate model of this type has several uses, e.g.: a) Identification of targets for metabolic engineering (Patil and Nielsen, 2005). b) Interpretation of transcription data and identification of regulatory features (David et al., 2006). c) Metabolic flux analysis (Christensen and Nielsen, 1999). d) Evaluation and improvement of gene annotation (Pel et al., 2007). e) Identification of drug targets (Thykaer et al., In review). In order to derive these models faster, reconstruction of genome-scale metabolic networks has often been based on an identification of enzymatic activities from the genome annotation (Förster et al., 2003, Duarte et al., 2004b, Borodina et al., 2005, David et al., 2006). While this is an efficient way of getting an initial list of reac-

tions, the approach does have a number of innate weaknesses, as discussed by Borodina et al. (2005). One major concern is that errors in the annotation cause false prediction of the presence of enzymes, which can affect the modeling results greatly. Some alleviation of this problem can be achieved with extensive curation afterwards (Borodina et al., 2005). An improvement of this is seen in the recent model for human metabolism by Duarte et al. (2007), who used a combination of genomic and bibliomic information, thus basing the network on peer-reviewed features. An additional advantage of including an extensive literature survey in the metabolic reconstruction is that it allows inclusion of characteristics, which do not have identified genomic features and are unique for the studied organism. Additionally, integrating data from literature reveals the inadequacies in our knowledge on metabolism, i.e. cases where specific steps in pathways have not been investigated. Finally, this approach creates linkages between the metabolic network of the specific organism and literature on the individual reactions, thereby providing a convenient topic-based index and direct reference to the relevant literature.

Based on manual curation of an extensive bibliomic survey of the literature on *A. niger*, the work of this chapter provides a comprehensive catalogue of all reported intracellular enzymatic activities in *A. niger* and thus establishes the entire metabolic network. Based on this, a stoichiometric metabolic model has been constructed. In addition to being useful for model simulation and data analysis as mentioned above, the model provides a link between reactions, genes and scientific papers, thereby representing a comprehensive database on most of the currently available information on the metabolic enzymes of *A. niger*.

3.1 Results

3.1.1 Reconstruction of the metabolic network

The reconstructed metabolic network of *A. niger* comprises 1190 biochemically unique reactions. These reactions are all interconnected with no gaps (missing reactions) in pathways. If reactions for isoenzymes are added based on the gene annotation, the total number is 2240 reactions. 52 enzyme complexes were identified in the network. 371 cited articles and 871 unique open reading frames (ORFs) are associated with the included reactions. The network comprises a total of 1045 metabolites distributed across three compartments; extracellular, cytosolic and mitochondrial. A summary of the support for the included reactions is shown in Figure 3.1. The full list of reactions with bibliography of the supporting articles is available in App. Table A.1 and the list of metabolites is given in App. Table A.2.

Biomass calculation

A key element of the model is to have a correct biomass composition as this defines the drain of metabolites into the pool of components constituting the biomass. Here the biomass composition for *A. niger* was calculated based solely on reported measurements. The overall biomass composition is found in Table 3.1. A more detailed description of the composition of the components of the biomass can be found in App. Tables A.3–A.8.

For modeling growth, key energetic parameters m_{ATP}, Y_{xATP} and the P/O ratios (see the method section for details) were calculated from published data. m_{ATP} was estimated to be $1.9\,^{\text{mmol ATP}}/_{\text{g DW}\cdot\text{h}}$. This is in agreement of the value found in the model of *A. niger* central metabolism by David et al. (2003). The cost of growth-associated maintenance (Y_{xATP}) was calculated to be $61\,^{\text{mmol ATP}}/_{\text{g DW}}$. The P/O ratios were set to 2.64 for mitochondrial NADH, and 1.64 for succinate and cytosolic NADH as in David et al. (2003).

Overview of the metabolism

The reaction network of *A. niger* comprises central carbon metabolism, catabolic pathways for 115 different carbon sources and 23 different nitrogen sources and anabolic pathways for the components of the biomass. Additionally, reactions for the production of glucoamylase and α-amylase have been added to allow calculation of the theoretical maximum yields and the ener-

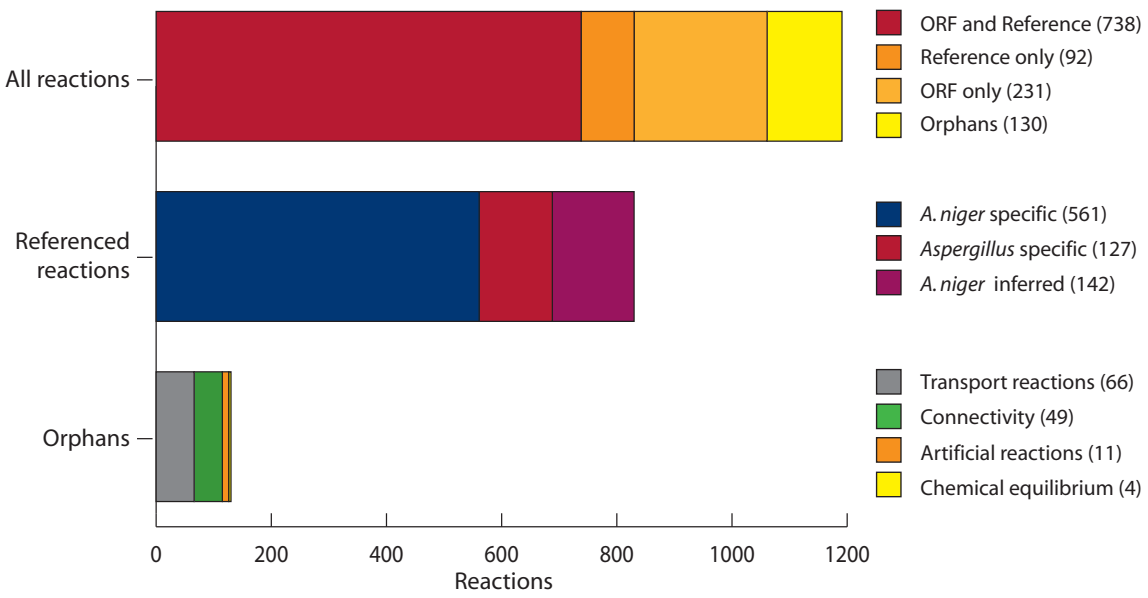

Figure 3.1: Statistics of the reconstructed *A. niger* metabolic network. Top bar shows the support for the 1190 included unique reactions. Middle bar shows the distribution of the references according to specificity. The bottom bar shows the reactions constituting the "orphans" — reactions with no supporting ORF or literature.

getic drain caused by producing these enzymes in high yields. As an example of secondary metabolism, a reaction for the biosynthesis of ochratoxin A has been included.

The 115 different carbon sources can be divided into 49 carbon sources found in literature to support growth (App. Table A.9), and 66 additional carbon sources that can support growth of the model (App. Table A.10). Included in these 115 carbon sources are more than 20 xenobiotic compounds. Of the 23 different compounds the model can use as a sole nitrogen source, 16 of these are described in the literature (App. Table A.11).

A number of pathways were assembled *de novo* for this model based on the available literature. For these, the pathways in the model represent a review of the present knowledge of fungal metabolism supplemented with inferred reactions. Some of the catabolic pathways for xenobiotic compounds hold examples of these inferred reactions, since for many of these; a complete pathway has not yet been hypothesized in fungi. Another example of this is the steroid biosynthesis, which has not been fully elucidated in fungi with all its co-factors. Based on a combination of reviews on other Aspergilli (Ferreira et al., 2005), fungi in general (Chopra and Khuller, 1984) and the SGD and KEGG pathway databases (Cherry et al., 1998, Kanehisa et al., 2002), a pathway for the biosynthesis of lanosterol, zymosterol and ergosterol has been reconstructed (Appendix A.4) and ORFs putatively assigned to the steps of the pathway.

To provide an overview of the metabolism, a metabolic map of the 1190 reactions in the model was drawn (Figure 3.2, full map is found in (Appendix A.1)). The design strategy and additional applications of this map will be discussed in detail in Chapter 4.

Supplementing reactions and metabolites

A small number of reactions reported in the literature were not included in the metabolic network (65 additional unique reactions). These reactions are activities that were not possible to connect to the rest of the metabolic model, e.g. catalysis of complex processes (such as multiple steps of biopolymer degradation of a single

Table 3.1: Biomass composition of *A. niger*. Note that the measurements compiled from literature accounts for nearly 98 % of the cell dry weight.

Biomass component	**References**	**Mass [g/g DW]**
Protein	Christias et al. (1975), Rockwell and O'Flaherty (1931), Smirnov and Chubova (1965), Terroine and Bonnet (2005), Imshenetskii et al. (1981)	0.263
DNA	Imshenetskii et al. (1981)	0.00244
RNA	Imshenetskii et al. (1981)	0.01814
Lipids	Brennan et al. (1974), Byrne and Brennan (1976), Chattopadhyay et al. (1985a), Morozova et al. (2002), Nemec and Jernejc (2002)	0.10899
Cell wall	Rockwell and O'Flaherty (1931), Smirnov and Chubova (1965), Imshenetskii et al. (1981)	0.38
Small molecules	Fuhrer et al. (1980), Promper et al. (1993), Witteveen and Visser (1995)	0.131
Ash	Nielsen et al. (2003b)	0.075
Sum		0.979

enzyme), or single enzymatic activities with no role in normal metabolism (such as bio-catalysis reactions). Additionally, 56 pathways were reported in literature, but not included. These are pathways for the biosynthesis of complicated secondary metabolites and catabolic pathways for complex aromatic substrates and share the feature that the end-product was reported in literature, but no information on the intermediate step(s) was available. However, as this catalogue of information still holds relevant information on the metabolic capabilities of *A. niger* it is included as App. Tables A.12 and A.13. References to the 87 articles describing these pathways and activities are included as well. Inclusion of these references brings the total number of citations up to 409. Furthermore, a detailed study and overview of extracellular polysaccharide-degrading reactions are found in chapter 9.

Assignment of ORFs

Upon manual inspection of the ORFs assigned from the annotation of the CBS 513.88 genome sequence, some irregularities were found: a) Only one inorganic diphosphatase (EC 3.6.1.1) was found in the genome sequence. For this reason, this ORF was assigned to both the cytosol and the mitochondrion. b) The same seven ORFs were assigned to the K+ and the Ca+ transporting ATPase, as these are difficult to separate based on sequence. The Na+, Mg2+ and other kation transporters may possibly be found within this group as well (MIPS category 67.04.01.02). c) Seven amine oxidases were found (four putative and three characterized). As the available literature does not correlate the reported activities to sequence or enzyme, all seven were assigned to the same reactions. d) For several general enzymes, a large number were found. These were alcohol dehydrogenases (20), amidases (14) and acid phosphatases (7). These were not possible to separate into specific functions based on sequence, but it is unlikely that they are all catalysing the same reaction with the same specificity, as the annotation may indicate.

To further expand the applications of the reconstructed network, ORFs from the genome sequence of *A. niger* ATCC 1015 (Baker, 2006) were assigned to the model as well. Of the 871 ORFs assigned to the model from the CBS 513.88 genome sequence, 792 had direct candidates in the *A. niger* ATCC 1015 genome sequence (more than 90 % identity and e-values below 10^{-75}. Another 18 ORFs had candidates with identity between 80 and 90 % and e-values below 10^{-75}. 3 more short proteins had an identity between 80 and 90 %. To improve the as-

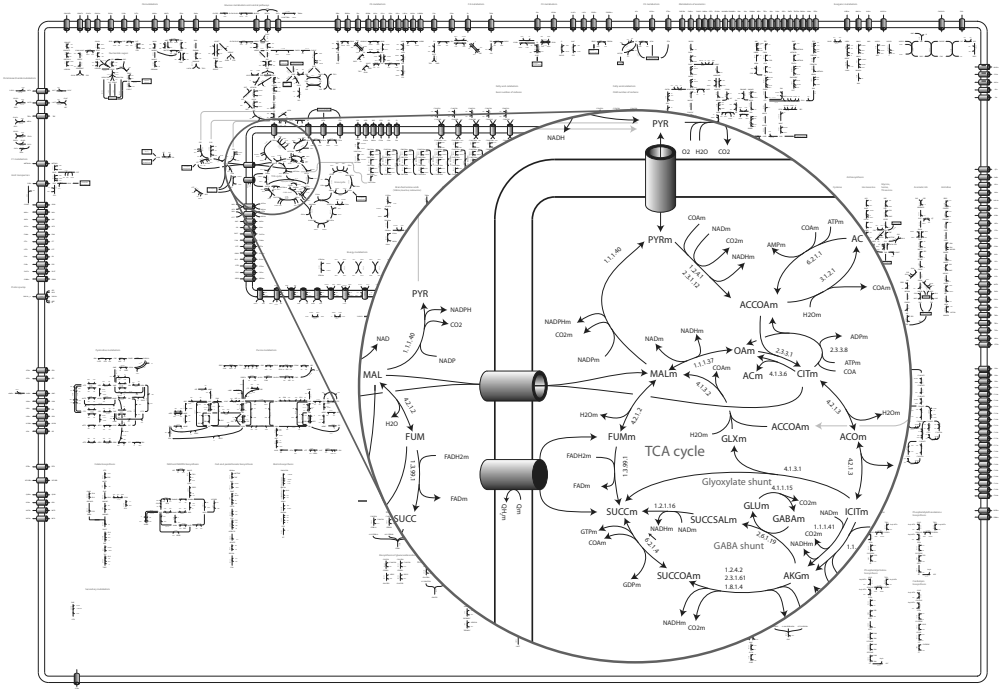

Figure 3.2: Reduced size version of a map of *A. niger* metabolism (Appendix A.1). An example of the level of detail is shown for the citric acid cycle.

signment, the results were examined manually, and an additional 31 ORFs were paired up. A total of 30 putative enzymes (3.5 %) in the *A. niger* CBS 513.88 genome were not found in the *A. niger* ATCC 1015 protein sequences. 21 of these were found at the nucleotide level using blastn (McGinnis and Madden, 2004), but were not present in the best gene predictions. The assignment of ORFs from both genome sequences to reactions is shown in App. Table A.1.

Comparison of fungal metabolic networks

The key statistics of the *A. niger* metabolic network were compared to that of other fungal stoichiometric models (Table 3.2).

To aid the reader, the naming convention proposed by Reed et al. (2003) for *E. coli* metabolic models has been adopted. Much like a strain number, the name of the organism is added a designation for the model with the following syntax: *i*XXy. *i* is for in silico, distinguishing it as a computer model and not a strain. This is followed by the initials (XX) of the person who developed the model, in this case *i*MA, and the number of ORFs (y) included in the metabolic network. Henceforth, the model presented in this study will be denoted as *A. niger i*MA871, or *i*MA871 as a shorthand form.

To evaluate the overlap of the metabolic network of the Aspergilli, the reactions in *A. niger i*MA871 were compared to a model of *A. niger* central metabolism (*A. niger i*HD20, David et al. (2003)) and a genome-scale model of *A. nidulans* (*A. nidulans i*HD666, David et al. (2006)). The results are shown in Figure 3.3.

93 reactions were found exclusively in *A. niger i*HD20. These are for the largest part lumped reactions and artificial reactions producing biomass. The remaining difference is mostly cases where the enzyme is present in both models, but the subcellular localization differs. *A. nidulans i*HD666 contains 209 reactions uniquely found in that network. These are to a large extent reactions relating to lipid synthesis, as this has been completely redesigned

Table 3.2: Comparison of key statistics of selected fungal stoichiometric model. The convention of naming the models has been adopted from Reed et al. (2003).

		Genes	Metabolites[a]	Unique reactions[b]
*S. cerevisiae i*FF708	Förster et al. (2003)	708	584	842
*S. cerevisiae i*ND750	Duarte et al. (2004a)	750	646	1149
*A. nidulans i*HD666	David et al. (2006)	666	551	794
*A. niger i*HD20	David et al. (2003)	20[c]	244	318
*A. niger i*MA871	This study	871	782	1190

[a]Number of chemically distinct metabolites, not counting presence in multiple compartments

[b]Unique reactions are defined as reactions being biochemically unique in their own compartment or transport reactions. Isoenzymes are thus not included in this number

[c]Reconstructed prior to the release of an *A. niger* genome sequence.

Figure 3.3: Venn diagram of reaction statistics for three *Aspergillus* models. The diagram shows the number of unique reactions shared and specific for the three models. Overlap between *A. nidulans i*HD666 and *A. niger i*HD20 was not investigated.

for *A. niger i*MA871. Additionally, a number of pathways found in *A. nidulans*, but not in *A. niger*, are included in these 209 reactions (e.g. aflatoxin, statins and penicillin biosynthesis). Most interestingly, the reactions found only in *A. niger i*MA871 are found all through metabolism, with the exception of the very central metabolism, thus suggesting that the bibliomic survey has been thorough, and that the model captures many activities unique for *A. niger*. The largest part of these reactions is found in the lipid biosynthesis and xenobiotic catabolism. A graphic overview of the unique reactions is presented in Appendix A.2.

3.1.2 Model validation

In order to evaluate the predictive capabilities of *A. niger i*MA871 and assess the inference of the modeling results, experimental results from articles were compared to the predictions of simulations of *A. niger i*MA871. The prediction of yields, the intracellular distribution of carbon-fluxes and physiological responses were examined. Additionally, transcription data was used to assess the network topology and the validity of the gene annotation.

Prediction of yields

A number of studies examine the yields of different products and biomass on substrates for cultivations of *A. niger*. A comparison of these to the predictions of *A. niger i*MA871 shows the following results: van de Merbel et al. (1994) reported production of 13 g/L oxalic acid from a mixture of 10 g/L glucose and 10 g/L fructose in 70 h. *i*MA871 predicts a theoretical maximum of a conversion of 100 % of carbon, giving 30 g/L oxalic acid. A review by Karaffa and Kubicek (2003) states that industrial citric acid producer strains can produce as much as 95 % citrate from sugar on a weight basis. *i*MA871 predicts a

Table 3.3: Comparison of biomass and oxygen yields for *A. niger* N402 (Schrickx et al., 1993) and *A. niger* *i*MR871. (*glaA*) denotes a mutant producing more glucoamylase. 95 % confidence intervals are given in parentheses. The "Carbon"-row shows the amount of carbon accounted for.

		N402	*i*MR871	N402 (*glaA*)	*i*MR871 (*glaA*)
Y_{xs}	(g DW/mol glucose)	100 (88.14–114.6)	105.5	96.29 (85.94–109.5)	105.1
Y_{xo}	(g DW/mol O_2)	54.68 (46.08–67.25)	60.6	54.14 (42.59–74.29)	60.6
Carbon		94.4 %	100 %	97.1 %	100 %

theoretical maximum of 98 % molar yield (app. 101 % on a weight basis). The molar yield of gluconic acid on glucose has been reported by Singh and Kumar (2007) to be as high as 98 %. Predictions by *i*MA871 give a theoretical maximum of 100 %. Based on the data presented by Schrickx et al. (1993), an examination of the prediction of glucoamylase over-production was performed. The study examines the growth of *A. niger* N402 and a glucoamylase over-producing mutant in continuous cultures and calculates the yields of biomass on glucose and oxygen for the strains. Simulations with *A. niger* *i*MA871 gives values that are 5–10 % higher than the yields reported by Schrieckx et al., but well within the given confidence intervals (Table 3.3). The slight over-prediction of the yields may be partially explained by the fact that the data in the article only accounts for 94–97 % of the carbon.

Modeling flux-distributions

The effect on the metabolic fluxes in central metabolism from deleting the gene encoding oxaloacetate hydrolase (*oahA*) has been measured by Pedersen et al. (2000b) using ^{13}C-labeling and a simplified model of the central carbon metabolism (40 reactions). To evaluate the predictive powers of *A. niger* *i*MA871 for flux-modeling, it was used to re-model the fluxes measured by Pedersen et al. (2000b). Modeling was done both for the wild-type results and the fluxes measured in the *oahA* deletion mutant. In both cases, the model was optimized for growth, with the measured values for citrate and oxalate from Pedersen et al. (2000b) set as constraints.

Initial modeling indicated that only 20 % of the glucose uptake was sent to the pentose phosphate pathway, which is low for a filamentous fungus, where values as high as 61 % has been reported for *Penicillium chrysogenum* (Henriksen et al., 1996). This under-estimation was due to a high activity of cytosolic $NADP^+$ isocitrate dehydrogenase, generating the necessary NADPH for synthesis of biomass components. The presence of this enzyme is established; the *in vitro* activity of $NADP^+$ isocitrate dehydrogenase was described by Muller (1975b) and found to be present in both the cytosol and the mitochondria in the publication of the *A. niger* CBS 513.88 genome sequence (Pel et al., 2007). Even so, it seems to be only slightly active in the cytosol under the conditions examined by Pedersen et al. (2000b). For this reason, a new round of modeling was conducted with the cytosolic activity of this enzyme limited to a low value, giving the flux distribution of Figure 3.4.

Examining the results of Figure 3.4, it is evident that the flux to the PP-pathway is still lower than the measured values, but in the same order of magnitude. For all measured fluxes, *A. niger* *i*MA871 predicts the direction of the response to the *oahA* deletion accurately, and the numerical size of the response in the simulation (i.e. the difference between the flux in the wild type and the mutant) generally approximates to the measured values. This is especially true for the fluxes towards biomass. *i*MA871 predicts the exact size of the perturbation in almost all cases, as well as the increase in total biomass yield by the deletion of *oahA*. When calculating the yield of NADPH on glucose, *A. niger* *i*MA871 accurately predicts a production of 100–120 mol NADPH/100 mol glucose, which is the yield reported by Pedersen et al. (2000b).

Modeling of physiological responses

One of the best studied physiological responses of *A. niger* is respiration during high-yield citrate production. A number of studies and reviews (Promper et al., 1993, Kirimura et al.,

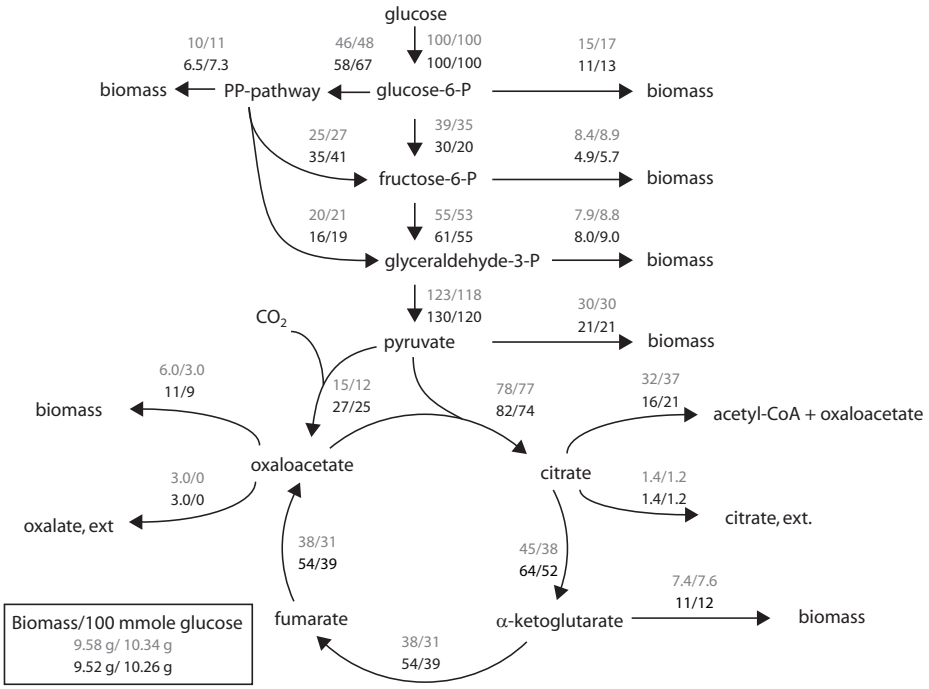

Figure 3.4: Comparison of measured *oahA* deletion fluxes to predicted values. The values in black are the calculated fluxes based on ^{13}C labeling, *wt*/Δ*oahA*. Gray values (upper) are predicted with *A. niger i*MA871. The figure was adapted from Pedersen et al. (2000b).

1999, Karaffa and Kubicek, 2003, Kirimura et al., 2006) have reported activity of both the cytochrome pathway and the alternative oxidase during citrate production. Additionally, it has been reported, that when the alternative oxidase is inhibited with salicylhydroxamic acid (SHAM), citric acid production is drastically decreased (Kirimura et al., 2006). Furthermore, it has been hypothesized that the alternative oxidase is present to remove excess NADH without production of further ATP (Karaffa and Kubicek, 2003). To study this response with *A. niger i*MA871, the fluxes through the oxidative pathways on different citrate yields were simulated (Figure 3.5), and the results do indeed show activity of the non-proton-pumping NADH-ubiquinone oxidoreductase and the alternative oxidase, when intermediate to high yields of citrate are obtained. However, at carbon yields above 98 %, the model predicts the use of other means to reduce the NADH excess. As yields this high have never been reported, the use of these may be an artefact caused by the true natural limitation being reached.

ORF assignment and network topology

To assess the validity of the reconstructed metabolic network of *i*MA871 and the ORFs assigned to the enzyme activities, the network was compared to transcription data published with the genome sequencing of *A. niger* CBS 513.88 (Pel et al., 2007). The transcription data are from the third day of a fed-batch cultivation with glucose and ammonium as carbon and nitrogen source, respectively. The presence/absence of mRNA from the relevant ORFs was plotted onto the metabolic map using the method of chapter 4 and visually inspected (Central metabolism in Figure 3.6, full map in Appendix A.3).

As seen from Figure 3.6, the succinate-CoA ligase complex is absent. Neither α- or β-chain of the complex is present, which suggests that an alternative pathway such as the GABA shunt is active. This is in coherence with reportings of Kumar et al. (2000c), showing the GABA-shunt

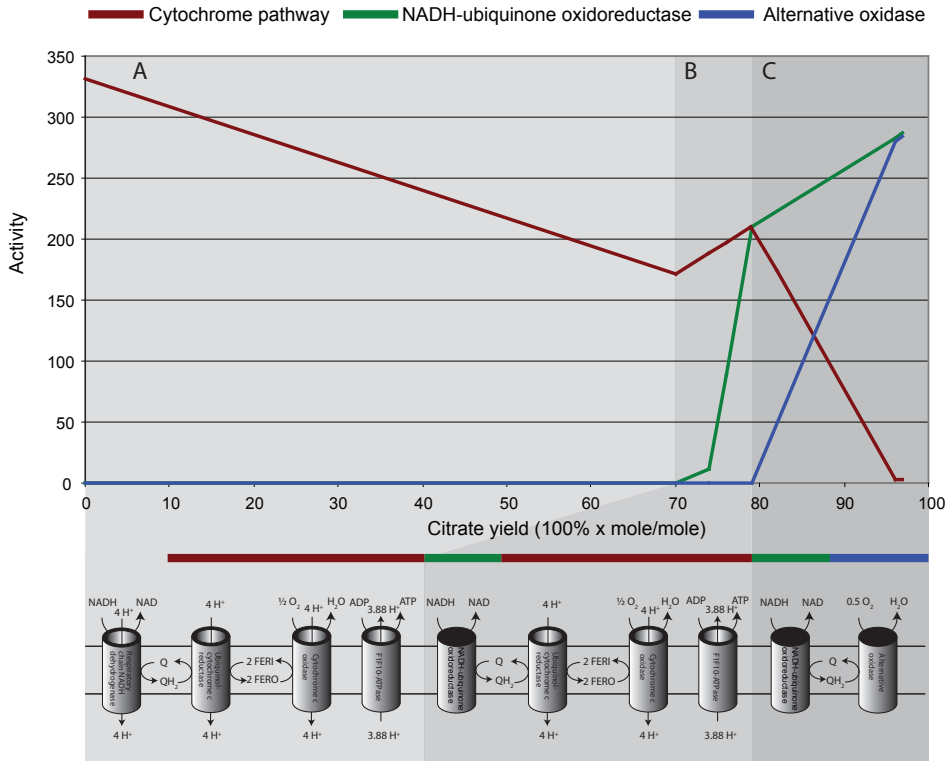

Figure 3.5: Predicted activities of respiratory pathways in citric acid fermentations. In phase A, the standard respiratory pathway is the sole source of NADH-turnover. In phase B, the proton-pumping NADH dehydrogenase is substituted for the non-proton-pumping NADH-ubiquinone oxidoreductase, resulting in a pathway that is a meld of the alternative oxidase pathway and the standard oxidative pathway. In phase C, the cytochrome pathway is substituted for the alternative oxidase pathway. The net result is a decreasing amount of ATP produced per metabolized NADH as the citric acid yield increases, resulting in a changing P/O ratio.

to be active during citric acid production.

Upon examining the remaining part of metabolism, it was found that the expressed genes correlated nicely with the pathways essential for biomass production. In no case were transcripts from an entire essential pathway found to be absent. Transcription of genes involved in polyol-synthesis for the biomass was also found to be active. All enzymes of the pathways producing coenzyme A, biotin, NADH/-NADPH and nucleoside phosphates were found to be present. All pathways not necessary for growth on glucose were found to be absent, with the only exception of the pathway from l-iditol to d-fructose. This includes catabolism of C_6-substrates other than glucose, C_5, C_4, C_3 and C_2 substrates and the urea and nitrate assimilation pathways. Transcription of the genes for a few enzymes in the middle of linear pathways were found to be absent, while the mRNA of enzymes up- and downstream in the pathway were present. These pathways were phosphocholine, cardiolipin, folate, lanosterol and ergosterol biosynthesis. This may be due to poor annotation of these genes, as there are a limited number of studies of these pathways in Aspergilli.

3.1.3 Assessing the metabolic capabilities of *A. niger*

As previously described, *A. niger* is widely used in industrial processes due to its innate ability

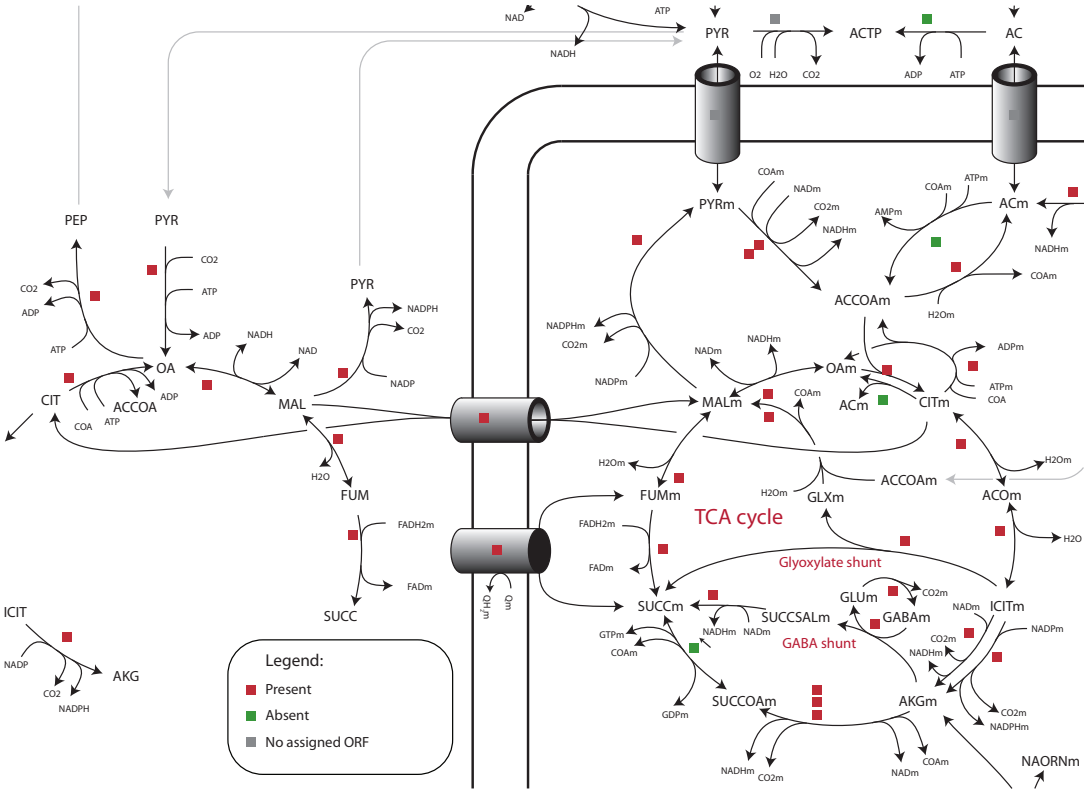

Figure 3.6: Enzymes expressed in central carbon metabolism when *A. niger* CBS 513.88 is grown on glucose. The full map is found in Appendix A.3.

to produce organic acids and enzymes in high yields. Using *A. niger* *i*MA871, the theoretical maximum yields of different metabolic precursors and acids from glucose were examined (Figure 3.7).

Panel A of Figure 3.7 shows that *A. niger* is highly efficient at producing all 12 essential precursor-molecules as defined by Stephanopoulos et al. (1998). The conversion these into amino acids is, as panel B shows, not completely efficient for all of the amino acids, but given the number of reduction equivalents necessary for synthesis of many of the amino acids, this is not surprising. It does, however, suggest that enzyme production yields may be increased by supplementing the medium with amino acids, especially the branched and the sulfur-containing amino acids. The plot of panel C demonstrates that *A. niger* is theoretically capable of converting glucose to a number of organic acids at 100 % efficiency, as has experimentally been demonstrated for several of the acids in the plot.

In addition to the compounds discussed above, the theoretical maximum yields of α-amylase and glucoamylase were calculated, giving 0.61 g α-amylase and 0.62 g glucoamylase per gram of glucose, respectively. Glucoamylase yields of 0.023 g/g have been observed in lab-scale fed-batch by Pedersen et al. (2000a), but commercial fed-batch fermentation yields are estimated to be 0.33–0.66 g/g in order to be economically feasible (L.L. Lasure, personal communications). This is in accordance with the model predictions.

3.2 Discussion

The metabolic network of *A. niger* has been reconstructed using a multi-omic approach. The reconstruction method was based on the labor-intensive approaches of a bibliome survey combined with extensive manual curation in every step of the process. A reconstruction of the *A. niger* metabolic network presented by Sun et al.

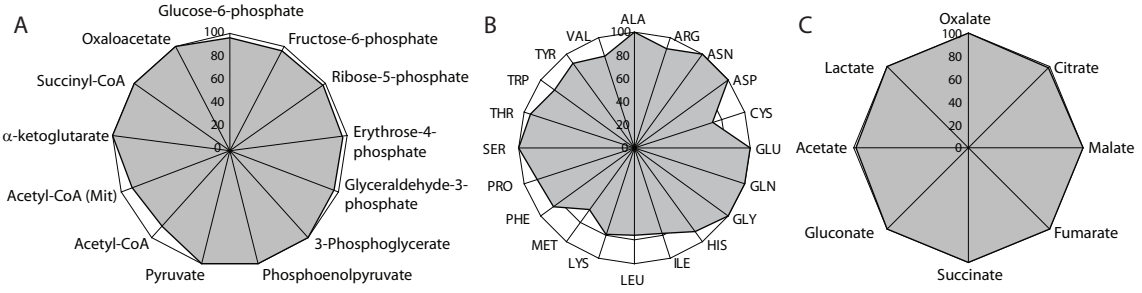

Figure 3.7: Radar plots of the theoretical maximum yields of selected metabolites from glucose and ammonium. The value axis shows percentage of C-moles of the metabolite from glucose. 100 % denotes a full conversion of glucose to the product. Panel A shows the twelve essential pre-cursor metabolites (Stephanopoulos et al., 1998). Panel B is the 20 common amino acids. Panel C shows selected organic acids.

(2007) was based on automated techniques with no curation or basis in features reported in literature. This study reports a network of approximately the same size as the network reconstructed here (998 unique EC numbers, 2443 reactions in total). Since the network of our study includes 1190 unique reactions and 2240 reactions in total, it is evident that manual reconstruction of the network can provide a validated result that is at least as comprehensive as the result of an automated approach, but with additional advantages such as the inclusion of citations. However, some caution should be taken in this comparison. The network of Sun et al. (2007) was constructed for comparison of metabolic features between fungi, and is thus not a metabolic model, does not contain any compartmentalization, and has a large number of reactions that are not connected to central metabolism. The network reconstructions thus have different scopes, and a comparison based solely on numerical stats may not do full justice to the unique features of each of the reconstructions.

The assignment of ORFs to reactions was based on the manual annotation of the *A. niger* CBS 513.88 genome sequence. While this is a conservative way of assigning ORFs to enzymatic functions, the number of genes assigned to a specific reaction may still be overestimated. In the case of general enzymes such as alcohol dehydrogenase (EC 1.1.1.1), it was not possible to differentiate between enzymatic specificities of the individual genes. Thus, all genes were assigned to the same reactions. This leads to an overestimation, meaning that the total number of 2240 reactions described above may be closer to an upper limit than the actual number. For this reason, we do not find that this is a useful statistic for comparing individual models.

For the purpose of communication of the presented model, and an easy overview of the model, a map of the metabolic network was prepared. However, since the map is prepared with a notation similar to the one known from biochemical textbooks, one may easily confuse it with these well-described pathways. It is important to bear in mind that the map is only a representation of the model, and a number of reactions are added for connectivity and are not based on reported experiments. One should always examine the relevant citations before drawing conclusions based on the metabolic map. With this in mind, it is an easily accessible reference tool for *Aspergillus* metabolism and future efforts in metabolic engineering.

The constructed model (*A. niger i*MA871) was based on the metabolic network and validated by several methods. A comparison of predicted yields of selected products compared to those yields reported in literature showed the model predictions to be in good accordance with experimental values. One exception was the prediction of the theoretical maximum yield of oxalate. However, since no strain optimization for oxalic acid production has ever been reported, the dis-

crepancy between experimental and predictive yields is not surprising. Oxalic acid is produced industrially through chemical processes (Wallace, 1926), and in the selection of most fermentation strains, it is sought to eliminate oxalic acid as a by-product (Hjort and Pedersen, 2000).

The prediction of flux distributions was examined by modeling the results of Pedersen et al. (2000b). While the overall prediction of biomass yields and perturbation effects were in good accordance with the measured values, in some cases, the numerical size of the fluxes were not. The sizes of the fluxes through mitochondrial fumarate and α-ketoglutarate are noticeably lower in the modelled results than in the measured results, while the flux from citrate to oxaloacetate and acetyl-CoA through a cytosolic pathway is higher in the prediction. Since the flux to cytosolic oxaloacetate is approximately the same amount too high as the flux to α-ketoglutarate is too low, it seems plausible that the problem is the flux distribution between TCA in the cytosol and mitochondria between the modelled and the measured values. This may be caused by the compartmentalization of reactions used by Pedersen et al. (2000b), as it is a lot less sophisticated than the one of *A. niger* *i*MA871. However, this is compensated for by Pedersen et al. (2000b) by the measurement of the labelling pattern in amino acids, which can estimate the carbon fluxes through the individual compartments. Another explanation might be that the difference in fluxes is an artefact of the *A. niger* *i*MA871 reconstruction process. In the compartmentalization of *i*MA871 reactions, a pathway was only placed in the mitochondria if evidence suggested that a part of it is located there. This means that the number of reactions assigned to the mitochondria of *A. niger* *i*MA871 is most likely lower than the actual number, thus decreasing mitochondrial carbon fluxes, and increasing cytosolic fluxes. While this artefact influences the flux distribution inside the cell, the nature of the model ensures that it does not affect the prediction of the "phenotype" of *A. niger* *i*MA871, such as product or biomass yields, as demonstrated by the results.

Using the example of oxidative phosphorylation during production of citric acid, we examined the prediction of physiological responses. Predictions were in good accordance with the known response of the different oxidative pathways. Interestingly, three modes of operation (phases A–C of Figure 3.5) were found. These allow a flexible regulation of the P/O ratio to dispose of excess mitochondrial NADH produced during high-yield citrate production. When examining these results, it is important to bear in mind that the results are very much dependent on the estimation of the P/O ratio of mitochondrial NADH included in the model parameters. The exact points of change from one phase to another, and the lengths of the phases, are not robust to changes in this value. One should therefore be careful in concluding at which yields a specific pathway is needed. However, the pattern of the phases, the order of them and the physiological response is robust towards changes in this value, and it is thus reasonable to believe that these systems are indeed in effect in *A. niger* during high yield production of citrate.

In conclusion, an integration of the genome, reactome, metabolome and bibliome of *Aspergillus niger* through reconstruction and modeling of the metabolic network is presented. With 70 % of the 1190 included reactions backed by literature from 371 articles, and above 80 % of the reactions associated with one or more of 871 assigned ORFs from the *A. niger* CBS 513.88 and the ATCC 1015 genome sequences (Baker, 2006, Pel et al., 2007), the network represents a comprehensive knowledge base for the metabolism of *A. niger*. A map providing a unique overview of the reconstructed metabolism in a format easily accessible to most researchers has been made. Stoichiometric modeling based on the metabolic network was validated with a wide array of data types. The systematization of data into the presented metabolic network and map has produced useful tools for examining system-wide data in a metabolic context. The included example of the network-aided interpretation of transcription data validates the gene assignments and demonstrates the potential of using the network for visualization and analysis of transcriptomic data. The presented modeling results produced new information on physiological traits of *A. niger* as well

as showing that *A. niger* has tremendous potential for being a versatile cell factory in the current development towards a bio-based economy.

3.3 Materials and Methods

3.3.1 Model reconstruction

The reaction list for *A. nidulans iH*D666 was purged of isoenzymes and used as a reaction template. An overview of the reconstruction procedure is shown in Figure 3.8. Initially, the *A. niger* bibliome was searched for references on metabolism, the bibliome being all articles concerning *A. niger* found on PubMed (`http://www.ncbi.nlm.nih.gov/entrez`) and on the ISI Web of Science. Information on enzymes/biochemical reactions, pathways, metabolites or biomass was manually extracted from the articles. The article references were added to the metabolic network reaction list. In addition to this, all literature references for *A. niger* enzymes found in BRENDA (`http://www.brenda.uni-koeln.de/`), the ExPASy enzyme database (`http://www.expasy.ch/enzyme`) and Swiss-Prot (`http://www.expasy.ch/sprot`) were examined, and added to the list of reactions as necessary. In some cases, reactions leading to the anabolism/-catabolism of a given metabolite were inferred from *A. niger* literature based on indirect observations (An example of this is the degradation of ferulic acid from the reportings of Milstein et al. (1988)).

Upon completion of the *A. niger* references from the bibliome and databases, the assembled information, representing lists of the reactome and metabolome, was examined for missing steps in pathways. If information on a given enzyme necessary for connectivity was lacking from *A. niger* literature, references to the reaction from other Aspergilli were added if available. After this step, information from KEGG (`http://www.genome.jp/kegg/kegg2.html`) was used to fill as many of the remaining gaps as possible. Gaps remaining after this were closed with the simplest possible reaction(s) (i.e. a dehydrogenation step or an elimination of water) resulting in a final network without gaps. Unless information existed stating otherwise, all reactions were defined as reversible. For modeling, some reactions were defined as irreversible due to artificial transhydrogenation cycles allowing NADH/NAPDH conversions. After the last reaction was added, extensive curation of the reaction list was performed. Reactions from the template *A. nidulans iH*D666 reaction list were removed, if no evidence existed for them in *A. niger*. The correctness of the individual reactions was checked by ensuring that C-, N-, O-, P- and S-balances as well as redox balances hold for all pathways and production of all biomass-components. After the metabolic network was compiled, ORFs were assigned to the included reactions.

ORF assignment

EC numbers in the annotation of the *A. niger* CBS 513.88 genome (Pel et al., 2007) were used to assign ORFs to the reactions of the metabolic network. No new reactions were added based solely on sequence information. This was supplemented by a manual examination of the ORF-reaction pairs. Homologues of the genes from the *A. niger* CBS 513.88 genome were found in the *A. niger* ATCC 1015 genome sequence (version 1.0) using blastp (McGinnis and Madden, 2004). The names of the ORFs from both genome sequences were added to the reaction list.

Biomass composition and growth energetics

To model growth, a biomass equation was added to the list of reactions. This equation acts as a drain of the component molecules used in growth. The biomass composition of *A. niger* was determined through a bibliome survey. A metabolite was added to the biomass equation if it was reported present in *A. niger* and the specific content quantified. The following energetic parameters were estimated: the ATP cost of growth-associated maintenance (Y_{xATP}), the ATP requirement for non-growth associated activities (maintenance) (m_{ATP}) and the operational P/O ratios. m_{ATP} was estimated using the relation between m_{ATP} , substrate consumption rate (q_s) and the specific growth rate (μ) described for continuous cultures of *A. niger* by

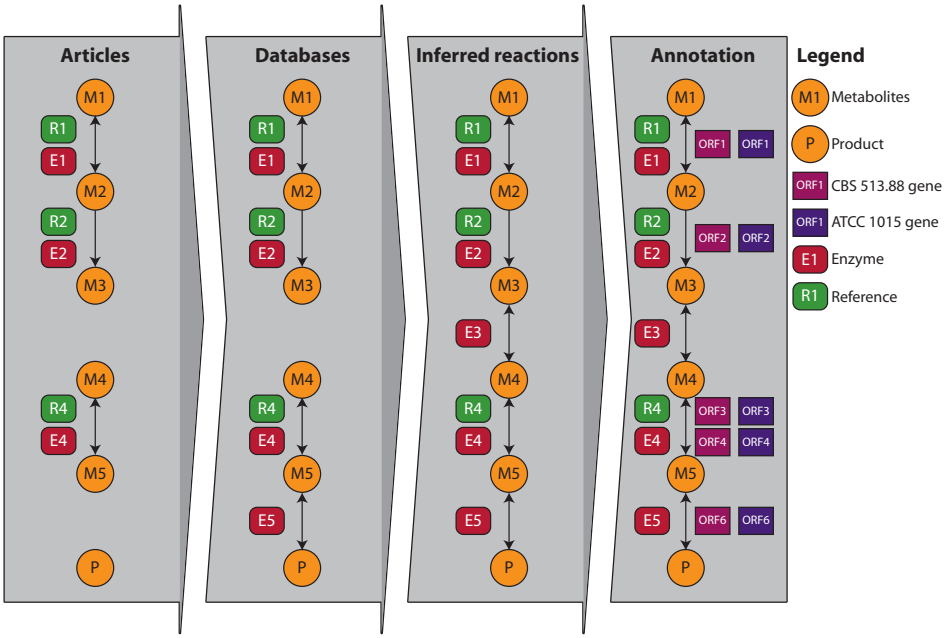

Figure 3.8: Overview of the model reconstruction process. Pathway addition was based on reported the presence of products and/or enzyme activities reported for *A. niger*. This was supplemented with enzymes reported present in other Aspergilli. Pathway and reaction databases (KEGG and BRENDA) was used where possible to fill gaps in pathways. If necessary, reactions were inferred to close the remaining gaps. Finally, ORFs were connected to reactions using the CBS 513.88 sequence annotation. No new reactions were added based solely on sequence information.

Schrickx et al. (1993). Y_{xATP} was calculated using the biomass yield on glucose in continuous cultures of *A. niger* from Pedersen et al. (2000a). The P/O ratios for the model were taken from the survey done by David et al. (2003).

Enzyme complexes

Enzymes that are part of a complex were identified by interrogating the *A. niger* CBS 513.88 annotation of the included proteins for the words "subunit", "chain'" or "complex". This information was added to the reaction list and used in the calculation of the number of iso-enzymes.

Compartmentalization and transport

The model has three compartments: extracellular space, cytosol and mitochondrion. Unless otherwise reported in literature, the enzymatic reactions were assumed to be cytosolic. When an enzyme was been reported to have isoenzymes in both mitochondrion and the cytosol, the compartmentalization predictions of the *A. niger* CBS 513.88 annotation were used to assign each ORFs to a compartment. Most transport reactions had to be inferred based on knowledge of reactions or pathways found in a specific compartment. To reduce the number of unsupported transport reactions, pathways have as a rule been assigned to the mitochondrion if one or more enzymes in the pathway were reported to be present there. Enzymes reported to be present in the cell wall were placed in the extracellular compartment. As there is little information in literature on peroxisomal localization for *A. niger* enzymes, this compartment was not included as a part of the model. Enzymes normally found in the peroxisome are therefore placed in the cytosol. One exception is the degradation of fatty acids, which in most fungi takes place in the peroxisome and the mitochondrion, with

an ill-defined distribution between the two. This has in the model been placed in the mitochondrion, along with the glyoxylate shunt.

3.3.2 Modeling

The quantification of metabolic fluxes was done using flux balance analysis (Schilling et al., 1999, Nielsen et al., 2003b, Stephanopoulos et al., 1998). The compiled set of metabolic reactions were converted to a stoichiometric matrix $\mathbf{S}$ of dimensions $m \times n$, where m is the number of metabolites and n the number of reactions or fluxes to be computed. Under the assumption that the metabolite-concentrations are in a pseudo-steady-state and the dilution effects from growth are negligible, the model can be represented as:

$$\mathbf{S} \cdot \mathbf{v} = 0 \tag{3.1}$$

where vector $\mathbf{v}$ represents the flux activity for each metabolic reaction. As the number of reactions (n) is greater than the m (the number of metabolites), the equation system is underdetermined. The system was solved using linear programming by formulating a specific objective (z). In the case of a maximization problem, the linear programming problem can be formulated as:

$$\max z = \mathbf{c}^T \cdot \mathbf{v} \tag{3.2}$$

$$\text{subject to } \mathbf{S} \cdot \mathbf{v} = 0 \tag{3.3}$$

$$\alpha_i \leq v_i \leq \beta_i \tag{3.4}$$

where $\mathbf{c}$ is a row vector containing the influence of the individual fluxes on the objective function z. The individual fluxes are constrained to the interval of $[\alpha_i, \beta_i]$. For irreversible reactions, either α_i or β_i are set to 0. In the case of reactions defining the limiting substrate, α_i and β_i are set to the same positive value. Unless otherwise stated in the text, the optimization parameter was maximizing flux through the biomass equation. Transport fluxes for phosphate, sulphate, ammonia/nitrate, and oxygen were not limited. For metabolites not present in the medium, the uptake rates (v_i) were set to 0. Secretion of all major metabolic products (organic acids, alcohols, amino acids, H_2O, CO_2 etc.) were allowed ($v_i \leq 0$). All calculations were performed using the commercially available software Lindo (Lindo Systems Inc).

Acknowledgements

Gerald Hofmann for valuable feedback in the construction process. Jette Thykær for good discussions on the technicalities of ^{13}C-labeling.

Chapter 4

ReMapper: a new tool for graphical representation of systems level data in a metabolic network

> “"What do you consider the largest map that would be really useful?"
> "About six inches to the mile."
> "Only six inches!" exclaimed Mein Herr. "We very soon got to six yards to the mile. Then we tried a hundred yards to the mile. And then came the grandest idea of all! We actually made a map of the country on a scale of a mile to a mile!
> "Have you used it much?" I enquired.
> "It has never been spread out, yet," said Mein Herr: "the farmers objected: they said it would cover the whole country and shut out the sunlight! So we now use the country itself, as its own map, and I assure you it does nearly as well."”
> *Lewis Carroll — Sylvie and Bruno Concluded*

The concept of systems biology, as described by Kitano (2002a), is based on a combination of information assembled by traditional studies of single cell components (the reductionist approach) and integration of this data in a manner to allow the investigation and elucidation of the dynamics of the biological system. Systems-scale or genome-scale approaches such as genomics, transcriptomics or proteomics are seen as methods for gaining information on the full system of the cell, and thereby making systems biology possible (Kitano, 2002b).

However, the interpretation of these types of data is notoriously complex, and tools are required for presenting data in a manner that can visualize the often thousands of numerical values that are generated by the genome-scale approaches. Several communities and research groups have risen to this challenge and developed tools that allow visualization of these types of data. A multitude of software packages and web-servers are available, and some of the best known are Pathway Tools (Karp et al., 2002), that allows the automated assembly of biochemical pathways from gene databases, Cytoscape (Shannon et al., 2003), originally developed for protein-protein interaction-studies, but adapted for a number of uses, and the web-service KEGG (Kanehisa et al., 2002), that compiles manually curated information on enzymes and pathways, and allows the plotting of reaction data onto the maps.

All the available software have individual design philosophies, with accompanying strengths and weaknesses. For example, the pathway mapping tool of KEGG is web-based, easy to use and interpret, but does not allow the use of custom metabolic networks, which is necessary when examining organisms not in the KEGG

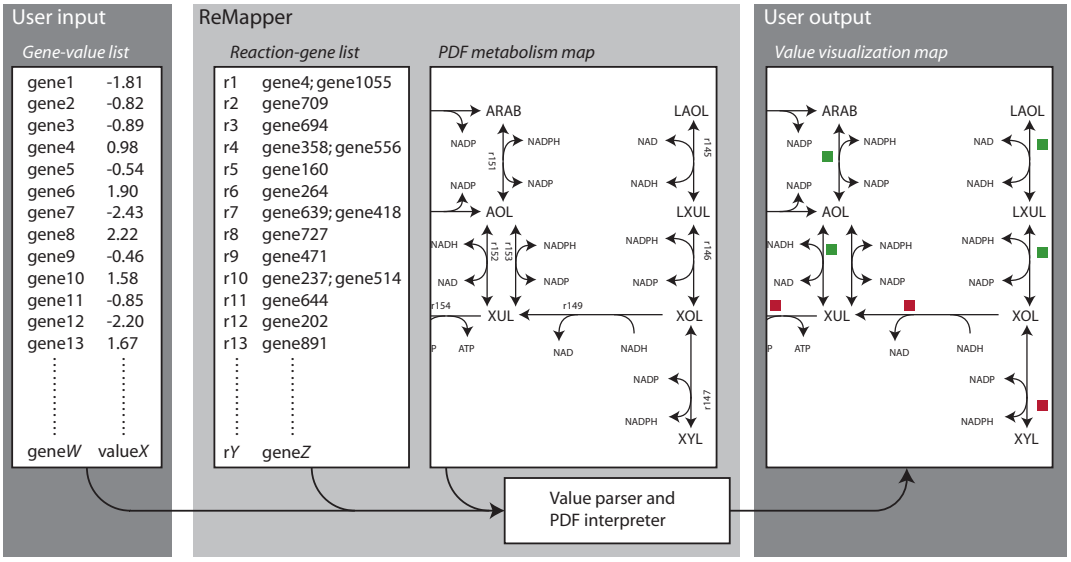

Figure 4.1: Overview of the information flow in a ReMapper session. The software receives a list of values associated with genes from the user, compares them to a list of reaction identifiers, and substitutes reaction identifiers (rXXX) on a metabolism map with boxes colored according to the value associated with the identifier. In the presented example, the xylose degradation pathway is up-regulated (red boxes).

database. Similarly, Cytoscape is capable of great flexibility and can be customized to almost any application, but is a complex software package with a steep learning curve and the output is not necessarily intuitive to interpret.

In the special interest of interpretation of modeling results, and data from industrial organisms, is the integration of genome-scale data with the biochemical network of the cell. In an extension of the reconstruction of the metabolic network of *A. niger* (chapter 3), development of a tool for metabolic network-aided data analysis of genome-scale experiments was wanted. Specifically, a tool was sought to comply with the following design criteria:

1. It should be based on metabolic networks from stoichiometric model reconstruction.

2. The interface should be intuitively accessible

3. Interpretation of the output should be intuitive and should not require specialized software

This resulted in the ReMapper software, a web-based service for the graphical representation of genome-scale data, as described in the following.

4.1 Implementation

4.1.1 Software architecture

The ReMapper software is written in Perl 5, with a HTML/CGI interface, and makes use of the Perl PDF manipulation library CAM-PDF-1.06 by Chris Dolan (available from `www.cpan.org`). Metabolic maps for the ReMapper as well as the output are provided in uncompressed Portable Document Format (PDF) version 1.6 (Adobe Systems Incorporated, 2004). The web version was tested to be compliant with the web browsers Internet Explorer 7.0, Firefox 2.0 and Safari 3.1.

4.2 Results

4.2.1 Overview

Using ReMapper, researchers can examine gene-based data in the context of metabolism. The software allows the input of genes with associated values, such as log fold changes from transcriptome studies, via a standard web interface and outputs the results as a PDF-file. The output is a highly detailed map of metabolism in the notation known from biochemistry textbooks with gene values plotted onto the map as color-coded boxes (Figure 4.1).

4.2.2 Maps

The software is in its first incarnation based on the map of *A. niger* metabolism presented in chapter 3 (Figure 3.2, Appendix A.1). Each reaction on the map has been assigned a unique identifier that can be recognized by the software (Figure 4.1). The identifiers/reactions are associated with genes based on the gene assignment from the reconstruction of the *A. niger* metabolic network. The ReMapper accepts gene IDs from both the genome sequence of *A. niger* CBS 513.88 (Pel et al., 2007) and *A. niger* ATCC 1015 (Baker, 2006). In addition to this, it is possible to plot gene-associated values from the genome sequences of *A. fumigatus* Af293 (Nierman et al., 2005), *A. nidulans* FGSC A4 (Galagan et al., 2005), and *A. oryzae* RIB40 (Machida et al., 2005) onto the map of *A. niger* metabolism. This is achieved by using bi-directional best blast hits between *A. niger* ATCC 1015 genes and the genes of other Aspergilli to correlated the genes of *A. fumigatus*, *A. nidulans*, and *A. oryzae* and to the reaction identifiers on the maps. The mapping software can separate the data on genes associated with the maps from the other genes of the genome, and is thus a quick way of gaining an overview of the transcriptome results.

The mapping possibilities have been extended with a map of *A. niger* extracellular polysaccharide metabolism has been added as well, which will be described in more detail in chapter 9.

4.2.3 Interface and options

The web-based interface (Figure 4.2) that can be accessed from `www.computationalbiology.dk/`, allows for the selection of three different options:

Map This option allows the selection of which map one wants to integrate data on. As described in section 4.2.2, two types of maps are available. Furthermore, for each map the input data can be supplied from a number of genome sequences.

Color scheme A selection between the often used color pairs red/green and orange/-green for positive/negative values. In case of the data being of the On/Off type (see the next option), the color used will be the first one (red or orange).

Values type The type of values one wants plotted to the genes. Up/Down for positive and negative values (mainly thought to be used for log2-ratios), and On/Off for values that are of a binary (0 or 1) nature (Such as the presence/absence of a gene in a group of interest).

Upon submission of the values, the software examines the data for format errors and presents a summary of the data before presenting a link to the visualization map (App. Figures B.1–B.2).

Besides the web-server implementation, two other versions of the software exist for implementation on local computers, one with similar graphical interface and one with a command-line interface (both available upon request).

4.2.4 Output

The output is presented in the form of the right panel of Figure 4.1 as a PDF-file that can be downloaded. For each reaction, the color coded box can assume one of five possible colors:

Red box All genes assigned to that reaction that were included in the query had positive values assigned to them (i.e. all present genes up-regulated).

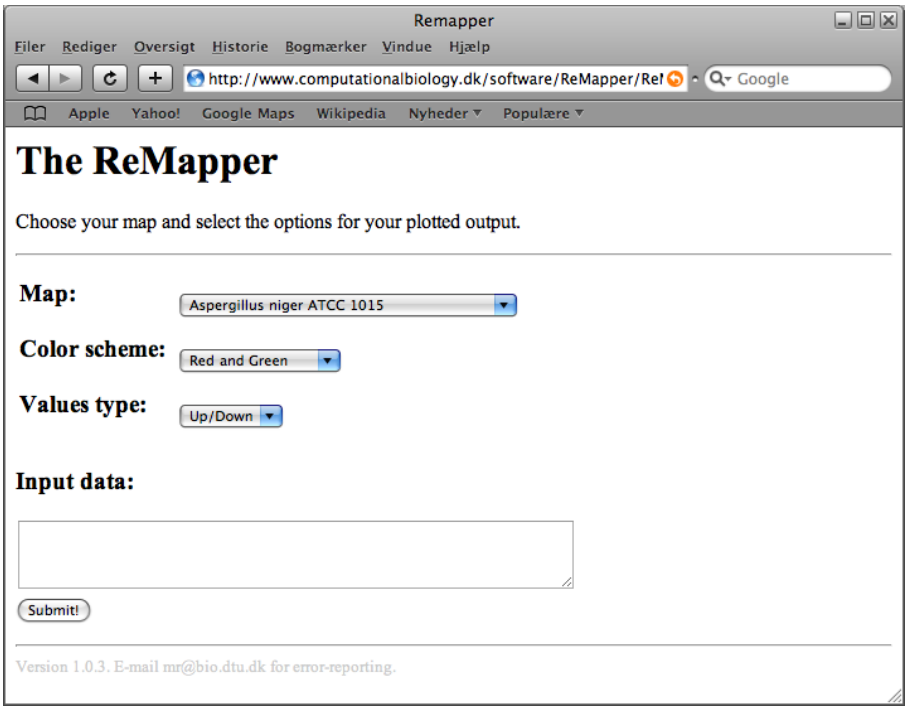

Figure 4.2: The ReMapper dialog box as it is presented in the Safari browser.

Green box All assigned values were negative (i.e. all present genes down-regulated).

Cyan box Both genes with positive and negative values are found in this group.

Gray box No genes have been assigned to this reaction. This would be the case when plotting genes from other Aspergilli onto the *A. niger* map and no bidirectional best hits were found.

White box No value was given for the genes of the reaction or the assigned values were 0.

A note on the algorithm of this assignment process is found in App. Table B.1.

Examples of the output figures are found throughout the chapters of this thesis (Most notably in chapter 9, and in Appendices E.2 and E.3) and in several submitted manuscripts (Panagiotou et al., Meijer et al., and Thykaer et al. as mentioned in the front matter of this thesis).

4.2.5 Extendability

The software is designed to make extension with other maps a simple matter. Chapter 9 presents an example of a new map. This makes extension only limited by the generation of new maps. Currently, maps have been made for *Corynebacterium glutamicum*, *Saccharomyces cerevisiae*, and *A. oryzae* which can easily be incorporated.

4.3 Discussion

A number of decisions were made in the design process. Initially, it was chosen to use a manually drawn map, rather than one that is reconstructed automatically from the model network using some of the available software packages. This decision was made based on initial studies using automatically compiled networks, where it was found that these had failings in two major areas. Firstly, network topology is very important when visualizing metabolic networks. Recognition of central pathways such as the citric acid cycle is easier if it is displayed as being round and gathered in one location. This was

difficult to reproduce in a manner that was instantly readable. Secondly, because of the first point, both interpretation and communication of results obtained in this fashion were challenging.

In order to make the map design process as easy as possible, it was decided to produce the maps in a format, where both reactions and the identifiers could be manipulated in a graphical interface (in contrast to for example basing it all on graphics defined in a text-interface), but where the results are saved as text files. For this, a number of suitable mark-up language based graphical formats/page definition languages exist and were considered in the process, e.g. Scalable Vector Graphics (SVG(World Wide Web Consortium, 2003)), Post Script (PS (Adobe Systems Incorporated, 1999)), Portable Document Format (PDF (Adobe Systems Incorporated, 2004)). In spite of advantages in the other formats, the PDF format was selected, as the target audience of the software is life scientists. PDF is the standard digital format for dispersement of scientific articles within the life sciences, and free PDF readers are readily available.

Finally, while the software was developed in a command-line interface, it was eventually integrated in a web environment. The internet offers easy access to the functionality without the need to install additional software, and is thus preferable to a command line interface or a stand-alone application to be installed on the users computer.

In conclusion, this study presents a tool for data-mining genome data in a metabolic context that is as simple in use as a web blast interface. The current version is solely applicable for analysis of data from studies of Aspergilli, but the technology is applicable to any study based on genetic data.

Acknowledgements

Chris Dolan for writing the CAM-PDF-1.06 Perl library and making it freely available. Intawat Nookaew, Kjeld Kjeldsen, and Wanwipa Vongsangnak are acknowledged for making maps of *S. cerevisiae*, *C. glutamicum*, and *A. oryzae* respectively.

Chapter 5

Design of an tri-*Aspergillus* custom GeneChip

> "As no better man advances to take this matter in hand, I hereupon offer my own poor endeavours. I promise nothing complete; because any human thing supposed to be complete, must for that very reason infallibly be faulty, I shall not pretend to a minute anatomical description of the various species or — in this place at least — to much of any description. [...] I am the architect, not the builder."
> *Herman Melville — Moby–Dick*

Recent advances in the Affymetrix GeneChip technology, specifically the increase in the physical densities of the nucleic acid probes, have allowed for having probes for the full set of predicted genes of several species in one chip design. One example is the Affymetrix GeneChip Yeast Genome 2.0 Array that allows for transcriptome analysis of both *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*. This micro array has in many respects superseded the previous versions containing only one of the species.

As described in chapter 2, the Aspergilli contains a number of species that are interesting in the scopes of both basic research and industrial applications. In the present study, it was sought to develop a tool for transcription analysis of *A. nidulans*, *A. niger* and *A. oryzae* based on the recent publication of the genome sequences of these three Aspergilli (Galagan et al., 2005, Baker, 2006, Pel et al., 2007, Machida et al., 2005).

5.1 Methods

5.1.1 Array type

The used array format was an Affymetrix CustomExpress Advantage Array of the 49-7875 format program, with 11 μm features, allowing for a maximum of 506,264 probes.

5.1.2 Genome sequences

Probe design was based on the coding sequences (CDS) of the predicted genes of the genome sequences of *A. nidulans* FGSC A4 version 3, (Galagan et al., 2005), the *A. oryzae* RIB40 sequence published by Machida et al. (2005), and *A. niger* ATCC 1015 version 1.0 (Baker, 2006). A collection of *A. oryzae* ESTs were added courtesy of Novozymes A/S. On the chip as well are probes for the genes of the *S. coelicolor* A3(2) (Bentley et al., 2002) genome. These were designed separately according to the protocol for prokaryotes, and using a method that will not be described here.

5.1.3 Probe design

For the initial design-phase, all probes were made using the OligoWiz 2.0 software as made available by Center for Biological Sequence Analysis — DTU (Nielsen et al., 2003a, Wernersson and Nielsen, 2005). This software calculates a list of optimal probes for every gene based on a number of specified parameters, including secondary structures and cross-hybridization in the specified genome sequence. The parameters were set to comply closely with the Affymetrix CustomExpress Array Design Guide (Downloadable from `www.affymetrix.com`). These parameters were set as follows:

Input file: For each genome, an input file was made containing all CDS from the genome in a fasta format. For *A. niger*, the sequence of the chymosin gene was added along with a number of polyketide synthases. The *A. oryzae* input file additionally contained the sequence of 1048 EST-sequences property of Novozymes. The *A. nidulans* data file also contained the sequence of the *Penicillium griseofulvum* 6-methylsalicylic acid synthase gene.

Species database: The input file(s) for each of the *Aspergillus sp.* were queried against sequence databases for the respective genome sequence on the OligoWiz server. These databases allow the selection of probes that are only found in unique locations in the genome, which reduces the extent of cross-hybridization.

Score parameters: The oligo-length was fixed to 25. The optimal melting point of the probes was determined by OligoWiz from the gene sequences based on a DNA:RNA model of the melting temperature of the DNA:RNA-hybridization product. Cross-hybridization was calculated using the default settings for eukaryotic probes of 24–26 nucleotides. This penalizes identities between 75 and 98 %. 100 % is not penalized as this would exclude the probe itself. The position preference was set to a 3'-preference due to the use of a poly-T primed labeling system for eukaryotic samples.

Probe numbers: For each gene, a maximum of 11 non-overlapping probes were calculated using the OligoWiz standard scoring of cross-hybridization, melting temperature, folding, position preference and low complexity.

5.1.4 Curation process

The curation phase was performed in cooperation with Affymetrix to make the probes comply fully with the specifications of the probe synthesis process. The full set of probe sequences were examined for duplicates, and those were removed using a custom Perl script. Duplicates are present in the initial output, as OligoWiz does not penalize for cross-hybridization between 100 % identical probes. In this case, it was decided to deviate from the Affymetrix standard protocol, as it recommends all but one of the identical probes to be removed. Removing all probes except one does not eliminate the risk of cross-hybridization, it only limits the effect to one gene, and for this reason, all duplicates were removed.

After running the script, the number of probes for each gene were examined. For all three Aspergilli, there were genes with no probes after the curation. The reason for this was the presence of multiple copies of the same gene in the genome or very short genes (<100 bp). Multiple copies of the same gene give the same optimal probes for all duplicates copies. The reason for the presence of identical copies is unknown. It seems unlikely that there are genes with exactly the same sequence present in the genome, so a more likely explanation is an error in the assembly/sequencing of the genomes.

To remedy this, all genes with less than three probes were examined, and the full probe sets were reinserted for those genes having significant blast-hits or an annotated function. When several identical copies of the same gene were present, only one was inserted, so that no duplicated probes were present in the final file.

Probes that the Affymetrix photolithography probe synthesis method was unable to produce were identified and shortened one base at a time using a custom Perl-script until it was possible to synthesize the probe.

5.1.5 Finalization

After the full list of probes was curated, standard Affymetrix hybridization control probe sets were added.

5.2 Results

5.2.1 Probe design statistics

A total of 380,738 probes to *Aspergillus* genes were designed. The curation included the removal of 2,529 probes to eliminate duplicates. 891 probes were shortened to accommodate limitation in the Affymetrix photolithography process.

5.2.2 Probe gene coverage

The finished design of the Affymetrix GeneChip includes probes for 99.5 % of the genes from *A. nidulans*, *A. niger* and *A. oryzae*. Due to the design criteria of having non-overlapping probes of similar melting points, not all genes have the maximum of 11 probes. An overview of the distribution of the number of probes per gene is found in Figure 5.1 (Numerical values in App. Table C.1).

5.2.3 Discussion

A number of different design decisions have been made. In this section, the major ones will be discussed. One such was the decision to have individual probes for each gene. Another design strategy for making the probes would have been to examine whether any genes from different species have sufficient homology to share a probe set instead of having individual probesets for all genes. This was discarded, as there is quite an evolutionary distance between the species. Galagan et al. (2005) calculates that the *A. nidulans* and *A. oryzae* species diverged $\sim$ 450 million years ago. It is therefore limited how many — if any — genes could share a full set. A similar situation is found in the Affymetrix GeneChip Yeast Genome 2.0 Array, where *S. cerevisiae* and *S. pombe* are present on the same array. Due to an evolutionary distance of $\sim$ 500 million years, separate probe sets have been designed for each of the genes. That this was a correct design decision was confirmed in the curation phase, where no genes in two different species were found to share all probes, and only 2,529 probes were removed due to duplicate sequences.

In the presented design, the cross-hybridization of probes was minimized by comparing the sequence of a possible probe with a OligoWiz database of the genome of the species. An alternative strategy would be to compare to a database containing sequence information from all three *Aspergillus* species. The advantage of this would be that in a given experiment using the chip, cross-hybridization to the probes of the species not being analyzed would be minimized. However, this would also make probe-design for genes that are 75–98 % similar between species difficult, as the probes of these genes would have high probabilities of being excluded due to the cross-hybridization scoring part of the algorithm. Also, by increasing the size of the database threefold, the chance of getting the best possible probe set for a given gene would be reduced. As the design is made for the analysis of mRNA from a single species, calculating cross-hybridization within one species should give therefore give the best possible result.

When calculating the probe position preference in OligoWiz, it is possible to choose a poly-T-primed scoring system instead of the 3'-preference chosen. This complies with the actual method used for labeling the cRNA, however, the scoring for the 3'-preference model is more in accordance with the position model used by Affymetrix in their design. For this reason, that option was chosen.

In conclusion, we have designed the array using state-of-the art technologies and software. Since the practice of having genes from multiple species on the same array is fairly new, due to the only recent increase in the probe capacity of the Affymetrix micro array technology allowing this, the procedure of how to do it is not yet standardized. However, it was prepared in accordance with the current practice, and as the application and validation of the next chapter will show, the obtained results are in line with

the expected trends and previously reported results.

Acknowledgements

Irina Borodina designed the probes for the *S. coelicolor* genes. Wanwipa Vongsangnak designed probes for the *A. oryzae* EST collection.

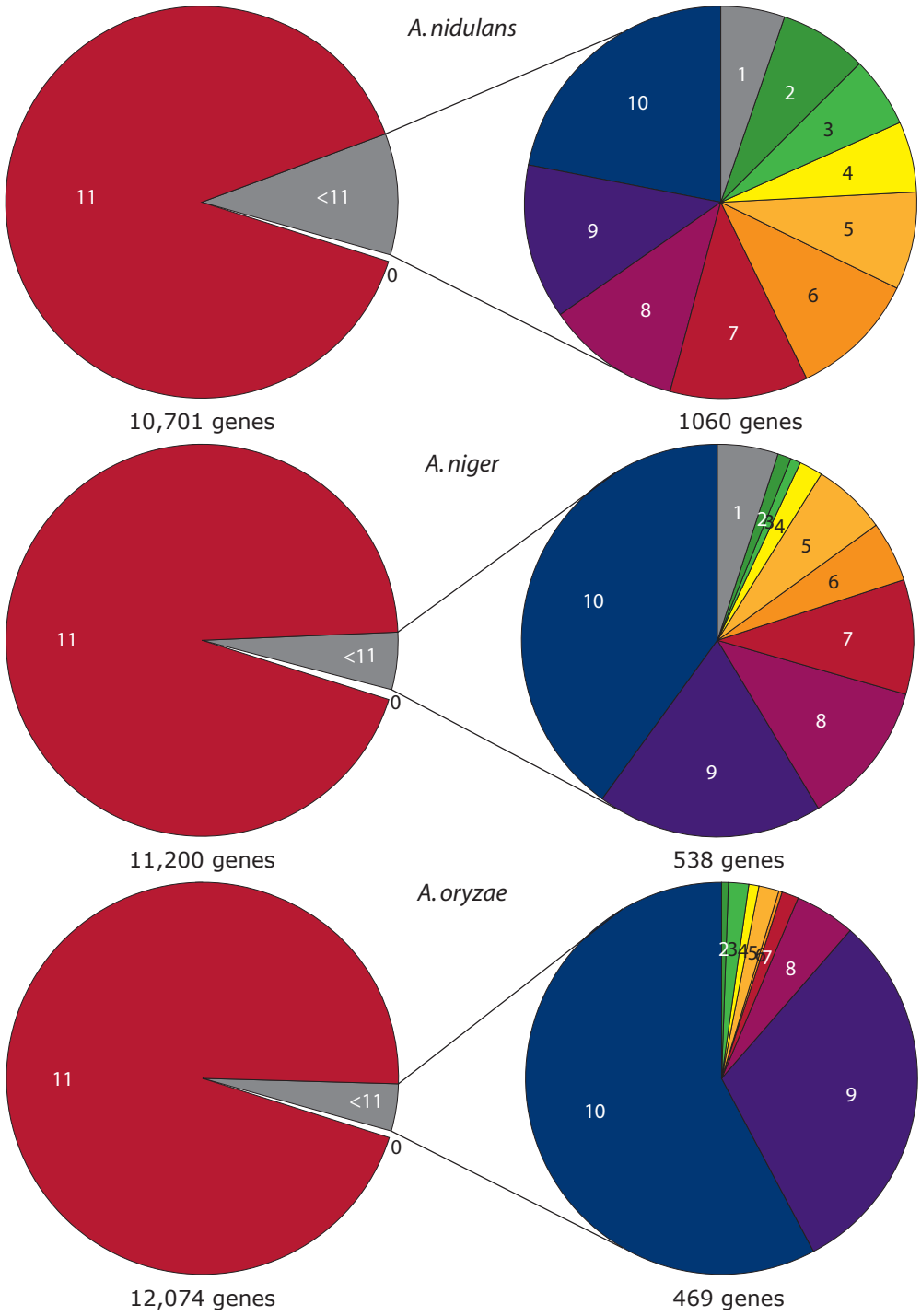

Figure 5.1: Pie charts of probe numbers for *A. nidulans*, *A. niger*, and *A. oryzae* genes represented on the designed microarray. The pie on the left shows the proportion of genes with the 11 probes versus those with less. The chart on the right shows the relative proportions of genes with a lower number of probes. The removed wedges marked with 0 represent genes not found on the array. The numerical values can be found in App. Table C.1.

Chapter 6

Validation and application of the tri-*Aspergillus* species GeneChip

> "If I have told you these details about the asteroid [B-612], and made a note of its number for you, it is on account of the grown-ups and their ways. When you tell them that you have made a new friend, they never ask you any questions about essential matters. They never say to you, "What does his voice sound like? What games does he love best? Does he collect butterflies?" Instead, they demand: "How old is he? How many brothers has he? How much does he weigh? How much money does his father make?" Only from these figures do they think they have learned anything about him."
> *Antoine de Saint Exupéry — The Little Prince*

As described in the previous chapter, an Affymetrix GeneChip was designed to allow analysis of genes from *A. nidulans*, *A. niger* and *A. oryzae*. While this design allows for analysis of individual species (as will be shown in chapters 7–9), it also has a potential for doing cross-species comparative transcriptomics. To validate the performance of the microarray for all three Aspergilli, and analyze evolutionally conserved carbon-source responses, triplicate batch cultivations on glucose and xylose media have been conducted for all three Aspergilli.

The validation was done in two parts, one examining the general characteristics of the probe-hybridization of the three Aspergilli, and another comparing the results of the statistical transcriptome analysis to published results. The main part of the study includes a methodology for conducting cross-species evolutionary studies within a genus using comparative transcriptomics.

6.1 Results

6.1.1 Array validation

In order to evaluate the effect of having probes for three species of the same genus on the same chip, one set of transcriptome data from each of the three species was randomly picked (See below for details on the experiments generating these data). For each experiment, the distribution of gene expression values for all three species was examined (Figure 6.1).

Expression values for the genes specific for the species from which the hybridized cRNA was isolated, are higher than expression values for genes from the other two Aspergilli. This is the case for samples from all three species. Even though *A. niger* and *A. oryzae* are more closely related to each other than to *A. nidulans*, this lineage was not reflected in the shape and levels of the distributions. This fact indicates that probes not targeting the genes from the species of the hybridized sample, are acting in an un-specific manner, much in the same way as do probes for un-expressed genes from the same species. Exceptions to this pattern are genes with high expression values in the non-hybridized species. These are comprised of constitutively highly ex-

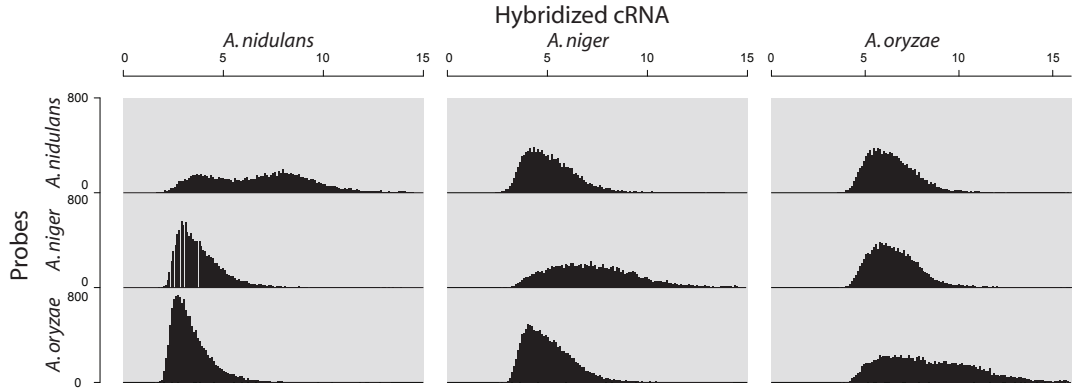

Figure 6.1: Histograms of gene expression values. The distribution of log2-transformed gene expression values of the genes of the three *Aspergillus sp.* in three experiments. Each column shows an experiment where cRNA from the noted organism was hybridized to the chip. Each row shows the distribution for genes from a specific organism. The analysis was done with the statistical software R (R Development Core Team, 2007).

pressed and highly conserved genes, specifically ribosome and histone components. While this issue influences the measured transcription levels, this should not affect evaluation of differential transcription between two sets of experiments, as the effect of the probes to the conserved genes will be the same between experiments.

6.1.2 Protein comparison

In order to examine systems regulating transcription conserved in all three Aspergilli, genes having homologues in all three species were identified using a blastp-based comparison. Using this approach, based on bi-directional best hits with an e-value cut-off of 1e-30, 5561 predicted genes were found to be conserved in all three species. The complete list is available from `www.computationalbiology.dk`. The number of genes with bi-directional, uni-directional, and no hits are shown in App. Figure D.1. The three sets of 5561 conserved genes (proposed 1:1:1 orthologues) were used for the further analysis of the transcript data.

6.1.3 Fermentation results

As a model example of experiments that can be conducted using the presented microarray, cultures of *A. nidulans*, *A. niger* and *A. oryzae* were prepared in well controlled bioreactors. All cultivations were batch cultures grown on defined salt medium with glucose or xylose as carbon sources. Each species had its own specific cultivation medium with a unique cultivation pH. For each of the three species, triplicate cultivations were preformed on each carbon source. Figure 6.2 presents a summary of the six sets of triplicates. Dispersed filamentous growth was observed throughout the fermentation for all cultivations.

6.1.4 Transcriptome analysis

For all three sets of glucose/xylose fermentations, statistical transcriptome analysis was performed. The significantly regulated genes in all three species were compared to the list of the 5561 conserved genes as well as with each other. This resulted in the identification of 23 conserved genes (Table 6.1) that are differentially regulated in all three species as well as 365 genes that are differentially expressed in only two of the Aspergilli (Figure 6.3). The 23 genes that are significant in all three can be seen as a conserved response across the *Aspergillus* genus.

A further inspection of the expression values of the 23 common genes revealed that the homologues are regulated in the same direction,

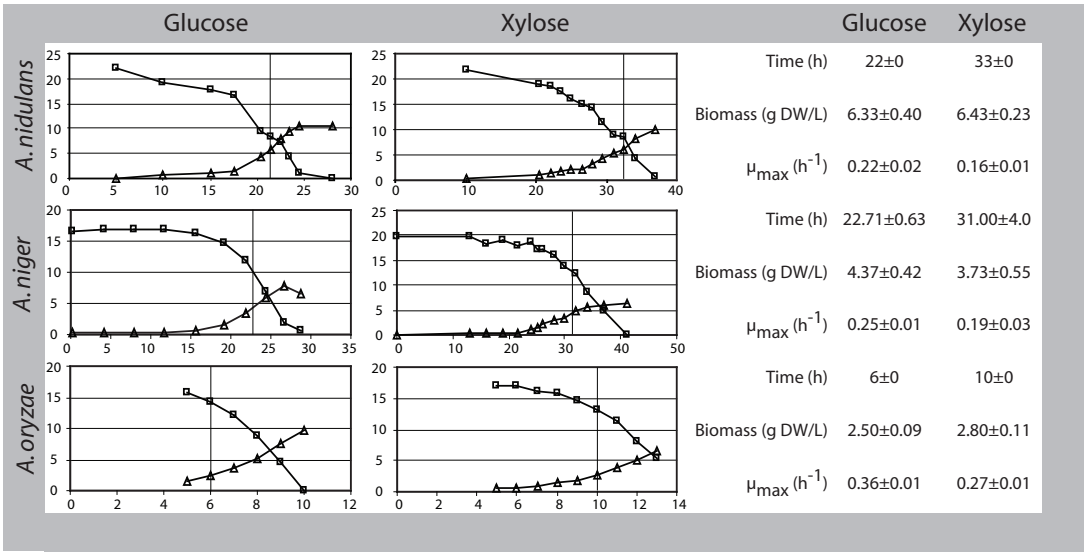

Figure 6.2: Summary of fermentation parameters. For each of the *Aspergillus sp.*, a profile of a representative replicate is shown. (□): Sugar concentration (g/L). (△): Biomass concentration (g DW/L). The vertical line shows the average time of sampling for transcriptome analysis. Time: Sampling time for transcriptome analysis. Biomass: Biomass concentration at the sampling time. μ_{max}: Maximum specific growth rate. For all values, averages and standard deviations for the three replicates are given.

with 22 of the genes being up-regulated on the xylose medium and only one gene being down-regulated.

The function of the genes in the less annotated *A. nidulans* and *A. oryzae* was inferred from the well-annotated *A. niger* genome sequence, based on the conserved sequences and conserved responses (Table 6.1). The majority of the 23 common genes are enzymes and sugar transporters. Specifically, the entire D-xylose degradatory pathway was induced in all three species (Figure 6.4). A low-affinity glucose transporter (*mstC*, described by Jørgensen et al. (2007)) was down-regulated, implying that this transporter has a higher affinity for glucose than xylose in all three species.

Interestingly, the xylanolytic transcriptional activator XlnR, previously only described in *A. niger* (van Peij et al., 1998b) and in *A. oryzae* as AoXlnR (Marui et al., 2002b), has a homologue in *A. nidulans* (AN7610), that is significantly induced on xylose as well. This suggests that the XlnR regulation is present in *A. nidulans* and functioning in a manner similar to that reported for *A. niger* and *A. oryzae*.

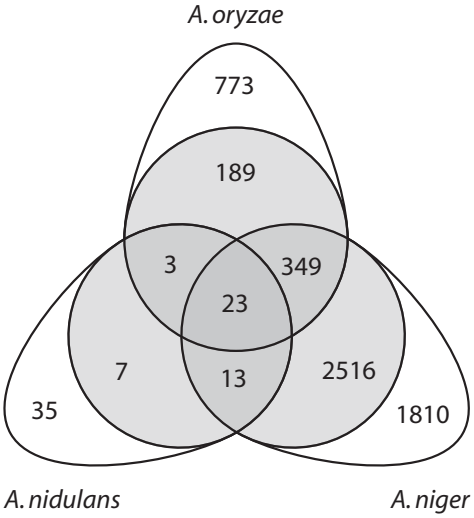

Figure 6.3: Venn diagram of differentially expressed genes. The gray circles contain the genes that are significantly differentially expressed and conserved in all three *Aspergillus* species. The numbers on a white background are not conserved in all three species, but still differentially expressed in a single species.

Table 6.1: 23 differentially expressed genes conserved in *A. nidulans*, *A. niger* and *A. oryzae*. Genes marked with "Up" in the Xylose column are up-regulated on xylose medium relative to glucose. The presence of motif A (5'-GGNTAAA-3') in the promoter region of the *A. nidulans*, *A. niger* and *A. oryzae* genes is marked with Nd, Ng and O respectively. Columns "Ng" and "O" give references to studies of XlnR induction in *A. niger* and *A. oryzae*. No references were found for *A. nidulans*. vanKuyk et al. (2001) show that *xkiA* is induced on D-xylose in *A. niger*, but not dependent on XlnR. The remaining references describe XlnR induction of the genes on D-xylose.

A. nidulans	***A. oryzae***	***A. niger***	***A. niger* annotation**	**Xylose**	**Motif A**	**Ng**	**O**
AN0250	AO090001000069	55668	Sugar transporter	Up	NdNgO		
AN0280	AO090005000767	55419	Glucosyl hydrolase	Up			
AN0423	AO090003000859	51997	D-xylose reductase (*xyrA*)	Up	NdNgO	Hasper et al. (2000)	
AN0942	AO090005001078	46405	L-arabitol dehydrogenase	Up	NdNgO		
AN10124	AO090003000497	213437	β-glycosidase	Up	Ng		
AN10169	AO090038000426	177736	Short-chain dehydrogenase	Up	NdNgO		
AN1677	AO090023000688	54541	Short-chain dehydrogenase	Up			
AN2359	AO090005000986	205670	β-xylosidase (*xlnD/xylA*)	Up	NdNgO	van Peij et al. (1998b,a)	Tsukagoshi et al. (2001), Marui et al. (2002b)
AN3184	AO090012000809	55604	Aldose 1-epimerase	Up	Ng		
AN3368	AO090010000208	212893	Glycoside hydrolase	Up	NdNg		
AN3432	AO090020000042	56084	Aldose 1-epimerase	Up	NdNgO		
AN4148	AO090009000275	205766	Sugar transporter	Up	NgO		
AN4590	AO090011000483	180923	Sugar transporter	Up	NgO		
AN5860	AO090026000494	197162	Monosugar-transporter (*mstC*)	Down			
AN7193	AO090023000264	55928	Aldo/keto reductase	Up	NdNgO		
AN7610	AO090012000267	48811	XlnR	Up	NgO		
AN8138	AO090010000684	212736	α-galactosidase	Up	Ng		
AN8400	AO090020000324	199510	Sugar transporter	Up	NgO		
AN8790	AO090020000603	209771	D-xylulokinase (*xkiA*)	Up	NdNgO	vanKuyk et al. (2001)	
AN9064	AO090038000631	203198	Xylitol dehydrogenase (*xdhA*)	Up	NdNgO		
AN9173	AO090010000063	194438	Sugar transporter	Up	NdNgO		
AN9286	AO090026000127	56619	α-glucuronidase (*aguA*)	Up	NdNgO	van Peij et al. (1998a), de Vries et al. (2002b)	
AN9287	AO090701000345	54859	Lipolytic enzyme	Up	NdNgO		

***cis*-acting elements** In recognition that one or more conserved transcriptional regulators might be active in all three species to produce the conserved response, statistical promoter analysis was performed on the 22 genes up-regulated on xylose for each of the three species. A 5'-GGNTAAA-3' motif (Motif A) was found to be significant (p=3.6e-28) and present 102 times in the promoters of 46 of the 3×22 genes (Table 6.1). In 12 of the 22 conserved genes, the motif was present in the promoter region of all three species. Included in these 12 sets of genes is the xylose catabolic pathway. For some of the genes (L-arabitol dehydrogenase and D-xylose reductase), the motif is found at the same distance from the start codon for all three homologues (within 5–20 bp) and with a different third base in each of the species. A preference for a specific third base in any of the species across promoters was not observed. This indicates an evolutionary pressure for maintaining the motif, but not the third base. Details on the location and sequence of the motifs are in App. Table D.1.

T 5'-GGCTAAA-3' motif has been reported to be the binding site for XlnR from *A. niger* and *A. oryzae*(van Peij et al., 1998b, Marui et al., 2002b). However, based on the statistical analysis, we are proposing that the 5'-GGNTAAA-3' motif is the original XlnR motif, and it has been conserved in *A. nidulans*, *A. niger*, and *A. oryzae*.

A separate analysis of the promoters that did not contain the XlnR-motif was carried out, but neither statistical analysis nor manual inspection for syntenic regions revealed any conserved domains. A similar analysis was performed for the down-regulated gene, but no significant motif was found.

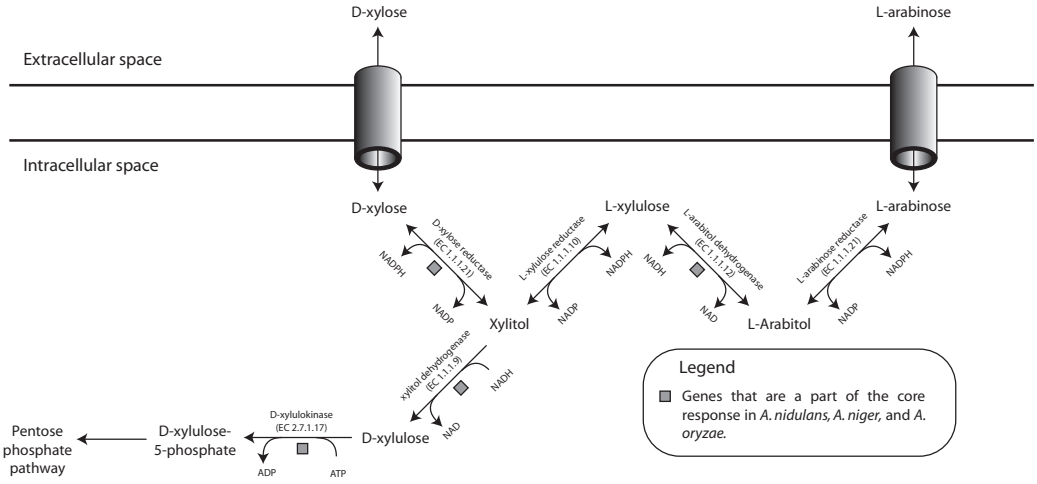

Figure 6.4: Overview of xylose and arabinose metabolism. Genes that are found among the core response of 23 genes of Table 6.1 are marked with gray boxes. The figure is based on information from de Groot et al. (2003).

Known XlnR-induced genes As a further validation of the method and the quality of the array, we examined the transcription levels of genes known to be induced by XlnR/AoXlnR on D-xylose. Genes found among the 22 sets of homologues have been marked with a reference in Table 6.1.

A multitude of genes are known from *A. niger*: xylanase B (*xlnB/xynB*, van Peij et al. (1998b,a)), arabinoxylan arabinofuranohydrolase (*axhA*, van Peij et al. (1998a)), acetyl xylan esterase (*axeA*, van Peij et al. (1998a)), ferulic acid esterase A (*faeA*, van Peij et al. (1998a), de Vries and Visser (1999)), endoglucanase A (*eglA*, van Peij et al. (1998a)), α- and β-galactosidase (*lacA*, de Vries et al. (1999a) and *aglB*, de Vries et al. (1999a)), cellobiohydrolase A (*cbhA*, Gielkens et al. (1999)), D-xylose reductase (*xyrA*, Hasper et al. (2000)), β-xylosidase (*xlnD*, van Peij et al. (1998b,a)), and α-glucuronidase (*aguA*, van Peij et al. (1998a), de Vries et al. (2002b)). Additionally has D-xylulokinase (*xkiA*, vanKuyk et al. (2001)) been reported to be induced on xylose, but not regulated by XlnR. All were found to be significantly induced in this study. Endoglucanase B and C (*eglB/C*) and cellobiohydrolase B (*cbhB*) are known to be induced by XlnR in *A. niger*, but not when grown on D-xylose (van Peij et al., 1998a, Gielkens et al., 1999, Hasper et al., 2002). These were not found to be significantly induced.

Fewer genes have been reported to be induced by XlnR on D-xylose in *A. oryzae*: β-xylosidase (*xylA*, Tsukagoshi et al. (2001), Marui et al. (2002b)), endoxylanases F1 (*xynF1*, Tsukagoshi et al. (2001), Marui et al. (2002b,a)), G1 (*xynG1*, Marui et al. (2002a)), and G2 (*xynG2*, Marui et al. (2002a)). All were significantly induced in *A. oryzae*. Endoglucanases A and B (*celA/B*) and cellobiohydrolases C and D (*celC/D*) are known to be induced by AoXlnR, but not when *A. oryzae* is grown on D-xylose (Marui et al., 2002a). These genes were not significantly induced here.

No genes have been reported to be induced by XlnR in *A. nidulans*, but the xylanases X22 (*xlnA*, Pérez-Gonzalez et al. (1996), MacCabe et al. (1998)), X24 (*xlnB*, Pérez-Gonzalez et al. (1996), MacCabe et al. (1998)), and X34 (*xlnC*, MacCabe et al. (1996a)) are known. Xylanases X22 and X24 are specific for acidic medium and alkaline medium, respectively, and only xylanase X24 was found to be induced. It had a p-value of 0.0527 and was thus not included among the 81 genes significantly regulated in *A. nidulans*. No reports were found where xylanase X34 was tested for induction on xylose, but MacCabe et al. (1996a) reported the induction on xylan.

In the study of this chapter, it was found to be significantly induced on D-xylose.

An overview of the expression values of the genes described above are presented in App. Table D.2.

In an examination of the above reporting, it is interesting that xylanases are found to be significantly induced on xylose in all three species, but not found in the core response of 22 genes. In a further examination, the xylanases do not have tri-directional best hits (They are found in the white areas of Figure 6.3). It thus seems that each species has a differentiated set of xylanases.

6.2 Discussion

In an application of the presented high-density microarray,a carbon source-based response conserved in three Aspergilli was identified. The design of the study, involving three different species, grown on three different defined minimal media, at three levels of pH, increases the likelihood of the found genes to be the true conserved "core" response to growth on xylose, and not responses relying on an extra factor in addition to xylose (with the possible exception of abundant oxygen). This approach also validates the argument that the xylanolytic transcriptional activator XlnR is a conserved system even though it has not previously been studied in *A. nidulans*. Backed by the finding that the 5'-GGNTAAA-3' motif is present and in some cases conserved as syntenic regions in all three species, it is proposed that the motif is indeed a XlnR-binding motif and conserved in *A. nidulans*, *A. niger*, and *A. oryzae*. As a point of interest, a study of the homologous genes and their promoter regions in *A. fumigatus* showed a XlnR-homologue to be present (Afu2g15620) and the presence of the 5'-GGNTAAA-3' motif in several of the other homologues, including the entire xylose catabolic pathway (App. Table D.3).

Upon further examination of the function of the up-regulated genes in *A. nidulans*, *A. niger*, and *A. oryzae*, it is interesting that the induction of L-arabitol dehydrogenase is found as a part of the core response. Since both our laboratory and that of Ronald de Vries (personal communications) have found minuscule amounts of arabinose in the commercial preparations of xylose, it might be an artifact. However, a further examination of the data shows that L-arabinose reductase (gene models AN1679, JGI46249 and AO090009000031), the first step in L-arabinose degradation (Figure 6.4), is not significantly induced in any of the three species. Additionally, the XlnR-motif is found in the promoter of L-arabitol dehydrogenase in all three homologues of the gene. This implies that this induction is not an artefact, and is indeed triggered by xylose. One hypothesis might be that L-arabitol dehydrogenase has an affinity for xylitol as well. Another hypothesis is based on, that in nature, xylose is seldom encountered alone, but as a constituent of hemicellulose, along with arabinose, galactose, glucuronic acid, mannose and other sugars (Pettersen, 1984, Carpita and Gibeaut, 1993). It is thus likely, that the fungi have evolved coupled responses. This also poses an explanation for the conserved induction of the multitude of sugar transporters, glucuronidase, epimerases, α-galactosidase and an array of glucoside hydrolases. It thus seems that the conserved xylose response is tailored to degrade complex carbohydrates such as hemicellulose, and D-xylose triggers this.

Another point of interest is that the promoter analysis suggests that *xlnR* is not autoinducible in *A. nidulans*. Additionally, the promoter analysis shows three sugar transporters in the core response, that only have the XlnR motif in *A. niger* and *A. oryzae*. This might imply that another less or non-conserved system is co-regulating the xylose/xylanolytic response in *A. nidulans* along with XlnR. Another possibility is that XlnR can bind to variations of the motif and is inducing more of the genes than the promoter analysis indicates. van Peij et al. (1998a) demonstrates that for *A. niger*, the last base of the motif can vary. de Vries et al. (2002b) describes induction via a 5'-GGCTAR-3' motif in *A. niger*. Marui et al. (2002b) describes the binding site to be 5'-GGCTA/GA-3' for *A. oryzae*. It is thus likely that each species has versions of the motif that are not statistically significant due to the increased variation, and these are facilitating the induction by XlnR. This in turn suggests that the

5'-GGNTAAA-3' motif is the original XlnR motif, upon which variations have developed since the branching of the individual species.

The low number of differentially expressed genes in *A. nidulans* might be interpreted as a lower sensitivity of the microarray towards the *A. nidulans* genes. However, manual inspection of the expression values show that this is due to a higher level of variation between the replicates of the *A. nidulans* cultivations. Other in-house experiments with *A. nidulans* and the presented arrays have identified more than 2500 significantly regulated genes and more than 1000 in a single comparison (Panagiotou et al., submitted), thereby showing that the array is sensitive towards a large number of genes. Additionally, the validation of the array using statistical analysis is confirmed by the expression patterns of hemi-cellulolytic genes known to be induced on D-xylose and/or by XlnR. These are in perfect accordance with the transcriptional analysis of this study.

With this study, access is given to a validated platform for analyzing transcription response in three different *Aspergillus sp.* This is the first array allowing analysis of the *A. oryzae* transcriptome and the first publicly available Affymetrix-based platform for transcriptome studies in any of the three species. Hopefully the publication will spur an increase of transcriptome analysis in the individual fungi, thus adding to the knowledge-base of this interesting genus of fungi. However, while the multitude of aspects that can be elucidated by traditional single organism transcriptome analysis are acknowledged, the largest potential of the herein presented microarray lies in studies of the multi-species type described in this study. It was demonstrated that the blast-based data-analysis strategy presented here can add strength to conclusions, and help identify systems and responses that are conserved across a genus. This possibility of studying the evolutionary depth of transcriptional regulation adds a new dimension to comparative transcriptomics.

6.3 Materials and Methods

6.3.1 Fermentation procedure

Strains

The strains used were *Aspergillus nidulans* FGSC A4, *A. niger* BO-1, and *Aspergillus oryzae* A1560, obtained from Novozymes A/S.

The *A. nidulans* stock culture was maintained on Sigma potato-dextrose-agar (PDA) at 4°C. *A. niger* was maintained as frozen spore suspensions at -80°C in 20 % glycerol. *A. oryzae* stock culture was maintained on Cove-N-gly agar at 4°C.

Growth media

A. nidulans batch cultivation medium: 15 g/L $(NH_4)_2SO_4$, 3 g/L KH_2PO_4, 2 g/L $MgSO_4{\cdot}7H_2O$, 2 g/L NaCl, 0.2 g/L $CaCl_2$ and 1 mL/L trace element solution. Trace element solution: 14.3 g/L $ZnSO_4{\cdot}7H_O$, 13.8 g/L $FeSO_4{\cdot}7H_2O$ and 2.5 g/L $CuSO_4{\cdot}5H_2O$. Carbon sources used were xylose or glucose monohydrate (20 g/L). *A.niger* complex medium: 2 g/L yeast extract, 3 g/L tryptone, 10 g/L glucose monohydrate, 20 g/L agar, 0.52 g/L KCl, 0.52 g/L $MgSO_4{\cdot}7H_2O$, 1.52 g/L KH_2PO_4 and 1 mL/L of trace elements solution. Trace element solution: 0.4 g/L $CuSO_4{\cdot}5H_2O$, 0.04 g/L $Na_2B_4O_7{\cdot}10H_2O$, 0.8 g/L $FeSO_4{\cdot}7H_2O$, 0.8 g/L $MnSO_4{\cdot}H_2O$, 0.8 g/L $Na_2MoO_4{\cdot}2H_2O$, 8 g/L $ZnSO_4{\cdot}7H_2O$. *A. niger* batch cultivation medium: Mineral base: 1.0 g/L $MgSO_4{\cdot}7H_2O$, 1 g/L NaCl, 0.1 g/L $CaCl_2{\cdot}2H_2O$, 0.05 mL/L antifoam 204 (Sigma) and 1 mL/L trace element solution. Trace element solution composition: 7.2 g/L $ZnSO_4{\cdot}7H_2O$, 0.3 g/L $NiCl_2{\cdot}6H_2O$, 6.9 g/L $FeSO_4{\cdot}7H_2O$, 3.5 g/L $MnCl_2{\cdot}4H_2O$ and 1.3 g/L $CuSO_4{\cdot}5H_2O$. Carbon sources used were xylose or glucose monohydrate (20 g/L). Nitrogen, sulfur and phosphate sources were 2.5 g/L $(NH_4)_2SO_4$, 0.75 g/L KH_2PO_4 (glucose medium) or 7.3 g/L $(NH_4)_2SO_4$, 1.5 g/L KH_2PO_4 (xylose medium). Concentrations were higher on xylose medium to avoid nitrogen starvation. *A. oryzae* spore propagation medium (Cove-N-gly): 218 g/L sorbitol, 10 g/L glycerol 99.5 %, 2.02 g/L KNO_4, 25 g/L agar and 50 mL/L salt solution. Cove-N-gly salt solution: 26 g/L LiCl, 26 g/L $MgSO_4{\cdot}7H_2O$, 76 g/L KH_2PO_4, 50 mL/L trace

element solution. Cove-N-gly trace element solution: 40 mg/L $Na_2B_4O_7 \cdot 10H_2O$, 400 mgL $CuSO_4 \cdot 5H_2O$, 800 mgL $FePO_4 \cdot 2H_2O$, 800 mgL $MnSO_4 \cdot H_2O$, 800 mgL $NaMoO_4 \cdot 2H_2O$, 8 g/L $ZnSO_4 \cdot 7H_2O$. *A. oryzae* medium for pre-cultures (G2-GLY): 18 g/L yeast extract, 24 g/L Glycerol 87 %, 1 mL/L Pluronic PE-6100. *A. oryzae* batch cultivation medium: 2.4 g/L $MgSO_4 \cdot 7H_2O$, 3.6 g/L K_2SO_4, 1.2 g/L citric acid monohydrate, 2.4 g/L KH_2PO_4, 3 g/L $(NH_4)_2HPO_4$, 1.2 g/L Pluronic acid (PE-6100) and 0.6 mL/L trace element solution. Trace element solution: 14.3 g/L $ZnSO_4 \cdot 7H_2O$, 8.5 g/L $MnSO_4 \cdot H_2O$, 13.8 g/L $FeSO_4 \cdot 7H_2O$, 2.5 g/L $CuSO_4 \cdot 5H_2O$, 3 g/L citric acid monohydrate (as a chelating agent) and 0.5 g/L $NiCl_2 \cdot 6H_2O$. Carbon sources used were xylose or glucose monohydrate (15 g/L).

Preparation of inoculum

A. nidulans A4 fermenters were inoculated with spores to a final concentration of 6×10^9 spores/L. The spores were cultivated on potato dextrose agar (PDA, Sigma) at 37°C for 4–5 days, and harvested by adding 20 mL of distilled water.

A. niger BO1 fermentations were initiated by spore inoculation to a final concentration of 2×10^9 spores/L (Glucose cultivations) or 5.7×10^9 spores/L (Xylose cultivations). The spores were propagated on complex media plates and incubated for 7–8 days at 30°C before harvest with 10 mL of 0.01 % Tween 80.

A. oryzae A1560 fermenters were inoculated with app. 60 g broth of *A. oryzae* A1560 cultured at 30°C for 24 hours on G2-GLY liquid medium in shake flasks at 250 rpm. The pre-cultures were inoculated with 5 mL of spore solution harvested from mycelium grown on Cove-N-gly agar at 34°C for 3–4 days. Spores were harvested with 0.1 % Tween 80.

Batch cultivations

A. nidulans batch cultivations were performed in 1.5 L bioreactors with a working volume of 1.2 L. The bioreactors were equipped with two Rushton four-blade disc-turbine impellers rotating at 350 rpm. The pH was kept constant at 5.5 by addition of 2 M NaOH or HCl and the temperature was maintained at 30°C. Air was used for sparging the bioreactor at a constant flow rate of 1 vvm (volume of gas per volume of liquid per minute).

A. niger batch cultivations on glucose medium were performed in 2 L Braun fermentors with a working volume of 1.6 L, equipped with three Rushton four-blade disc turbines. The bioreactor was sparged with air and the concentrations of oxygen and carbon dioxide in the exhaust gas were measured in a gas analyzer. The temperature was maintained at 30°C. The pH was controlled by automatic addition of 2 M NaOH. Agitation and aeration were controlled throughout the cultivations. For inoculation of the bioreactor the pH was set to 2.5, stirring rate 100 rpm and aeration 0.1 vvm. After germination, the stirring rate was increased to 300 rpm and the air flow to 0.5 vvm. 11–12 hours after inoculation, the stirring rate was increased to 600 rpm and the air flow to 1 vvm. When the CO_2 in the exhaust gas reached a value of 0.1 %, the stirring rate was set to 1000 rpm and the pH was gradually increased to 4.5.

A. niger batch cultivations on xylose medium were carried out in 5 L reactors with a working volume of 4.5 L. The bioreactors were equipped with two Rushton four-blade disc turbines and pH and temperature control. Inlet air was controlled with a mass flowmeter. The temperature was maintained at 30°C and the pH was controlled by automatic addition of 2 M NaOH. The pH was initially set to 3.0 to prevent spore aggregation; only when spores started to germinate the pH was gradually increased to 4.5. Similarly, the stirring speed was initially set to 200 rpm and the aeration rate to 0.05 vvm. After germination, these parameters were progressively increased to 600 rpm and 0.89 vvm and kept steady throughout all the rest of the fermentation.

A. oryzae batch cultivations were done in 2 L fermenters with a working volume of 1.2 L. The stirrer speed was kept at 800 rpm during the first 4 hours, and then increased to 1100 rpm. The pH was maitained at 6.0 by addition of 4 M NaOH and 4 M HCl and the temperature was maintained at 34°C. The aeration flow rate was set at 1.2 vvm. Dissolved oxygen tension was initially calibrated at 100 %.

The concentrations of oxygen and carbon dioxide in the exhaust gas were monitored with a gas analyzer (1311 Fast response Triple gas, Innova combined with multiplexer controller for Gas Analysis MUX100, B. Braun Biotech International).

Sampling

Cell dry weight was determined using nitrocellulose filters (pore size 0.45 μm, Gelman Sciences). The filters were pre-dried in a microwave oven at 150 W for 15 min or at 100°C for 24 h, cooled in a desiccator and subsequently weighed. A known volume of cell culture was filtered and the residue was washed with distilled water or 0.9 % NaCl and dried on the filter for 15 min in a microwave oven at 150 W or at 100°C for 24 h and cooled in a desiccator. The filter was weighed again and the cell mass concentration was calculated. These values were used to calculate maximum specific growth rates. For gene expression analysis, mycelium was harvested at the mid-late exponential phase by filtration through sterile Mira-Cloth. At this point, *A. niger* mycelium was washed with a phosphate buffered saline (PBS) buffer (8 g/L NaCl, 0.20 g/L KCl, 1.44 g/L Na_2HPO_4 and 0.24 g/L KH_2PO_4 in distilled water). The mycelium was quickly dried by squeezing, and subsequently frozen in liquid nitrogen. Samples were stored at -80°C until RNA extraction.

Quantification of sugars and extracellular metabolites

The concentrations of sugar in the filtrates were determined using HPLC on an Aminex HPX-87H ion-exclusion column (BioRad, Hercules, CA). The column was eluted at 60°C with 5 mM H_2SO_4 at a flow rate of 0.6 mL/min. Metabolites were detected with a refractive index detector and a UV detector.

6.3.2 Transcriptome analysis

Extraction of total RNA

A. nidulans and *A. niger*: 40–50 mg of frozen mycelium was placed in a 2 mL microcentrifuge tube, pre-cooled in liquid nitrogen, containing three steel balls (two balls with a diameter of 2 mm and one ball with a diameter of 5 mm). The tubes were then shaken in a Retsch Mixer Mill at 5°C for 10 minutes, until the mycelium was ground to powder. Total RNA was isolated from the powder using the Qiagen RNeasy Mini Kit, according to the protocol for isolation of total RNA from plant and fungi.

A. oryzae: Total RNA was purified by using the Promega RNAgents Total RNA Isolation system according to the protocol. For the purification, approximately 1 g of frozen mycelium was ground to a fine powder under liquid nitrogen using a ceramic mortar and pestle.

For all samples, the quality of the total RNA extracted were determined using a BioAnalyzer 2100 (Agilent Technologies Inc., Santa Clara, CA, USA) and the quantity determined using a spectrophotometer (Amersham Pharmacia Biotech, GE Healthcare Bio-Sciences AB, Uppsala, Sweden). The total RNA was stored at -80°C until further processing.

Preparation of biotin-labeled cRNA and microarray processing

Fifteen μg of fragmented biotin-labeled cRNA was prepared from 5 μg of total RNA and hybridized to the 3AspergDTU GeneChip (Available from Affymetrix upon request, order no. 520520F) according to the Affymetrix GeneChip Expression Analysis Technical Manual(Aff, 2007).

cRNA was quantified in a spectrophotometer (same as above). cRNA quality was assessed using a BioAnalyzer. A GeneChip Fluidics Station FS-400 (fluidics protocol FS450_001) and a GeneChip Scanner 3000 were used for hybridization and scanning.

The scanned probe array images (.DAT files) were converted into .CEL files using the GeneChip Operating Software (Affymetrix).

Analysis of transcriptome data

Affymetrix CEL-data files were preprocessed using the statistical language and environment R (R Development Core Team, 2007) version 2.5. The probe intensities were normalized for background using the robust multiarray average (RMA) method (Irizarry et al., 2003) us-

ing only perfect match (PM) probes. Normalization was performed subsequently using the quantiles algorithm (Bolstad et al., 2003). Gene expression values were calculated from the PM probes with the medianpolish summary method (Irizarry et al., 2003). All statistical preprocessing methods were used by invoking them through the affy package (Gautier et al., 2004).

Statistical analysis was applied to determine genes subject to differential transcriptional regulation. The limma package (Smyth, 2004) was used to perform moderated t-tests between the two carbon sources for each of the three species. Empirical Bayesian statistics were used to moderate the standard errors within each gene and Benjamini-Hochberg's method (Benjamini and Hochberg, 1995) to adjust for multi-testing. A cut-off value of adjusted p<0.05 was set to assess statistical significance.

Normalized and raw data-values are deposited with GEO as series GSE9298.

6.3.3 Comparison of protein sequences

The amino acid sequences of the predicted genes from each of the three genomes were compared to those of the two others using blastp (McGinnis and Madden, 2004) with an e-value cutoff of 1e-30. For each protein query sequence that gave one or more positive hits, the best hit was selected based on score (A uni-directional best hit). Bi-directional best hits were found by comparing the lists of best hits for two species against each other and selecting genes where the best hits paired up, thus giving a conservative set of 1:1 homologues for all pair-wise comparisons. So-called "Tri-directional" best hits were found by comparing the lists of bi-directional hits for all comparisons, and selecting the genes that had a 1:1:1-relationship in all comparisons between all three species (See App. Figure D.1).

6.3.4 Detection of conserved motifs

Conserved motifs were identified using R 2.5.1 (R Development Core Team, 2007) with the cosmo package v 1.2.0 (Bembom et al., 2007). Default settings were used with the following exceptions: A background Markov model was computed using the intergenic regions from scaffold 1 of the *A. niger* ATCC 1015 genome sequence. Intergenic regions containing unknown bases (N's) were pruned from the training set amounting to 1.7 Mb in 1214 sequences. The Two-Component-Mixture (TCM) model was used to search for conserved motifs. The maximum number of sites were increased to include all 102 sites. For all query-sequences was used 1000 bp up-stream of the start codon of the gene, or, in the case of some *A. niger* genes, 1000 bp up-stream of the predicted transcription start. Only 120 bp was available of the AN4590 promoter.

p-values were calculated as $P(X \leq n)$, with X being a Poisson-distributed stochastic variable with $\lambda = 0.418$ and n being the number of motifs found pr. kb. λ was calculated as the number of the conserved motif found pr. kb of the intergenic training set.

Acknowledgements

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Chapter 7

Genome-based comparative studies of *Aspergillus niger* ATCC 1015 and CBS 513.88

> "I'd say she is as pretty as you, but how do you compare two sunrises?"
> *Robert Jordan — A Crown of Swords*

A. niger has the rare characteristic that it is very efficient in producing two fundamentally different products, namely extracellular polysaccharide-degrading enzymes (particularly amylases) and organic acids (mainly citric acid). As discussed in sections 2.2.1–2.2.3, both types of products are of great commercial importance and have been the targets for extensive studies and metabolic engineering. Furthermore, a commercial and basic research interest in the *A. niger* species exists, and has driven the whole-genome sequencing of three different *A. niger* strains (see section 2.1.1).

Even so, only an in-depth analysis of the genome sequence of the industrial enzyme-producing *A. niger* CBS 513.88, has been published (Pel et al., 2007). While this information has been highly valuable, and initiated a number of new genome-based initiatives (Sun et al., 2007, Yuan et al., 2008a,b, Andersen et al., 2008a,b) as predicted by Cullen (2007), there is still a need for uncovering the fundamental differences between an acid-producing strain and an enzyme-producer.

The object of this chapter is to present the genome sequence of the citric acid-producing *A. niger* wild type strain ATCC 1015 and compare the strain to *A. niger* CBS 513.88, a high-yield producer of the extracellular enzyme glucoamylase (Pel et al., 2007). Often, in genome comparison studies, focus is on synteny analysis, sequence statistics and studies of groups of predicted genes. This has also been the case in this study, but to further explore the production characteristics of the two strains, studies of the fermentation physiology and transcriptome profiling of these fermentations have also been included. Special focus has placed on uncovering traits defining either producer strain. Furthermore, in interest of understanding single-gene mechanisms, and to aid metabolic engineering for applications in biotechnology, a comprehensive catalog of detailed gene-for-gene differences between the two strains have been made using a new blast-based analysis method (the Imprint algorithm).

This multi-disciplinary comparative analysis has identified a number of factors on multiple levels that are indicative of specialization as an acidogenic or an enzyme-producing strain, and has given new information on a surprising diversity of the *A. niger* species.

7.1 Results

7.1.1 General genome statistics

Version 1.0 of the *A. niger* ATCC 1015 genome sequence has been made available at the JGI interface for genome browsing (`http://genome.jgi-psf.org/Aspni1/Aspni1.home.html`). This

interface includes an overview of automatic and manual annotation. 11,200 genes were predicted in *A. niger* using several gene predictors. Gene model characteristics are summarized in Table 7.1.

Table 7.1: General genome statistics for *A. niger* ATCC 1015 and *A. niger* CBS 513.88. Except for genome sizes and the number of gene models, all values are averages.

	ATCC 1015	CBS 513.88
Gene models	11,200	14,165
Genome size (Mb)	34.85	33.9
Gene length (bp)	1696.1	1572
Transcript length (bp)	1501.3	N/A[a]
Protein length (aa)	484.3	439.9
Exons per gene	3.1	2.57
Exon length (bp)	480.8	370
Intron length (bp)	93.8	97

[a]Transcript length was not predicted for the CBS 513.88 sequence

In total 7752 *A. niger* genes (69 %) are supported by ESTs including 1577 (14 %) supported by full length cDNA sequences. The absolute majority (10,631, or 95 %) of the genes show sequence similarity to other proteins from the NCBI non-redundant protein set. 8216 gene models contain InterPro domain(s) (Zdobnov and Apweiler, 2001), including 6165 with predicted PFAM domains. Gene Ontology terms (Ashburner et al., 2000) were assigned to 6098 predicted genes (4641 assigned to a biological process, 5685 to a molecular function, and 2333 to cellular component). For 1590 genes, an EC number was predicted (527 unique EC numbers). 4390 genes were assigned in terms of eukaryotic orthologous groups (KOGs, (Koonin et al., 2004)). Of these, 1671 belong to cellular processes, 1129 to information storage and processing and 2434 to metabolism categories. More than 2100 gene models have been subject to manual annotation. The finished contigs (24 in total, spanning 34.85 Mb) were acquired from the JGI and will be made available from NCBI upon publication. Thus, the *A. niger* ATCC 1015 sequence is nearly complete with only 15 gaps (8 of these are centromeric regions) versus the published CBS 513.88 (Pel et al., 2007) which contains 485 gaps. One megabase (Mb) of ATCC 1015 genome sequence (2.5 % of the full genome) is not found in the *A. niger* CBS 513.88 genome sequence.

7.1.2 Synteny study

Based on the substantial research on linkage groups in *A. niger* (Bos et al., 1989, Debets et al., 1989, 1990a,b, Swart et al., 1992, Verdoes et al., 1994) and the supercontig orientation of Pel et al. (2007), the 24 contigs were arranged into eight chromosomes. Where telomeres were sequenced, these were used to orient the arms of the chromosomes (Figure 7.1).

A comparison (Figure 7.1) of the ATCC 1015 assembly to the published genome data of Pel et al. (2007), reveals a number of differences the genome configuration. Firstly, more than 500 kb of the extra one Mb of sequence in the ATCC 1015 assembly is located in four large gaps on chromosomes II, III and V. Secondly, the right arm of chromosome VI is oriented in the reverse direction of what was reported for CBS 513.88. Thirdly, a large section of chromosome VIII has been inverted. Fourthly, major rearrangement of the left arms of chromosomes III and VII has occurred. Both the rearrangement and the inversion have been confirmed with PCR spanning the breakpoints (data not shown). The same configuration as in ATCC 1015 is found in the genome sequence of ATCC 9029, also known as N400 (sequenced in a 4x coverage by Integrated Genomics). This implies that the chromosomal arrangement of CBS 513.88 differs from that of a typical *A. niger* strain. A model of the chronology leading to the rearrangement is proposed in App. Figure E.1. This rearrangement implies that the genetic markers of the left arm of Chromosome III reported by Debets, are actually transferred to chromosome VII of CBS 513.88. This has lead to an accidental attachment of Chr. VII L to Chr. III and vice versa in the genome publication of Pel et al. (2007). The presented configuration also explains a discrepancy reported by Pel et al. (2007) between the known sizes of chromosomes III and VII (Verdoes et al., 1994) and the sizes calculated from the genome sequence of CBS 513.88.

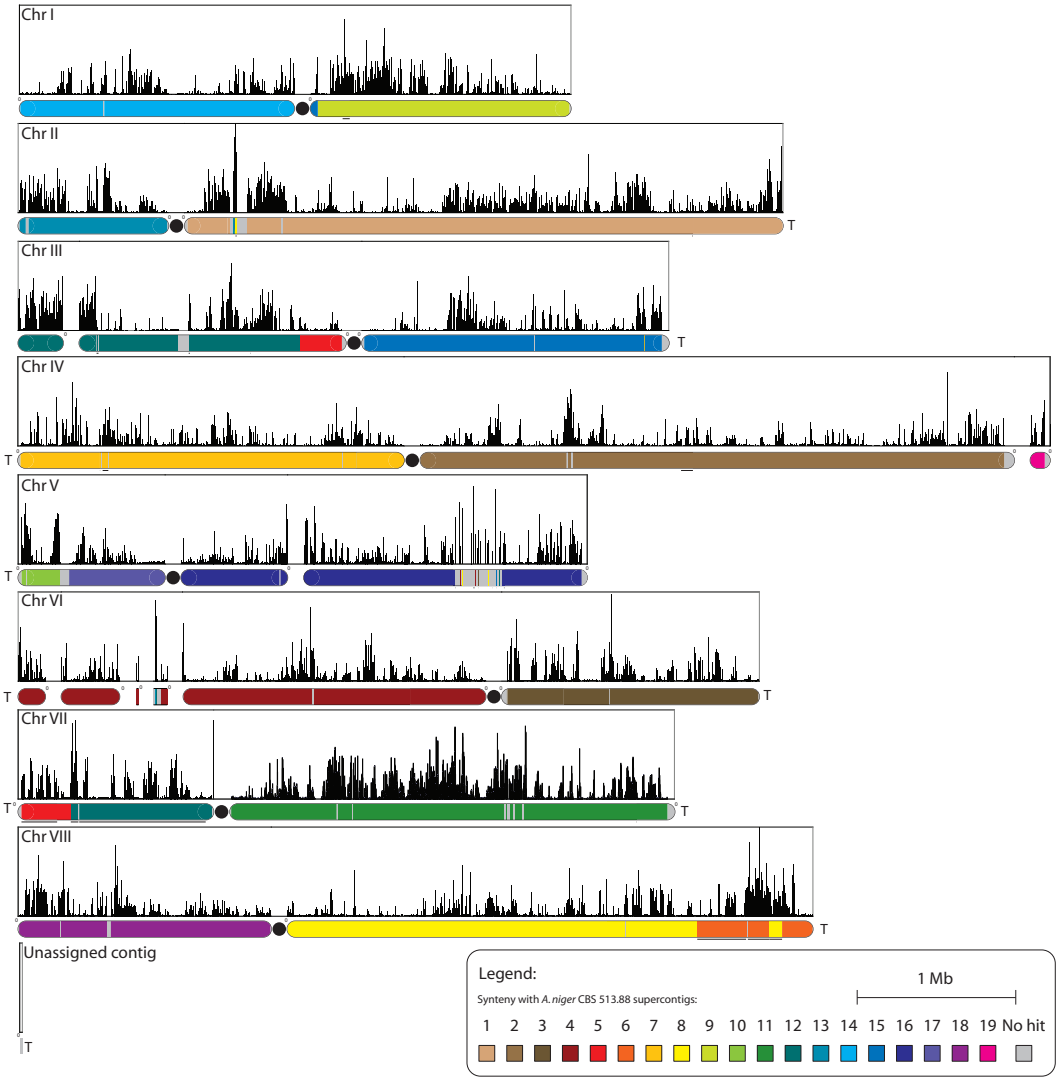

Figure 7.1: Synteny map of the contigs of A. niger ATCC 1015 to the supercontigs of A. niger CBS 513.88. The coloring of the chromosomes shows syntenic regions in A. niger CBS 513.88. Arabic numerals show the number of the supercontig in A. niger CBS 513.88. Gray areas shows regions not found in the CBS 513.88 sequence (Pel et al., 2007). Proposed locations of centromeric regions are shown with filled black circles. Sequenced telomeres are marked with a T. Zeroes mark the first base of the contigs. Black lines underneath the contigs denote sequence inverted in CBS 513.88. Black histograms show SNPs/kb (number of single nucleotide polymorphisms/kb) between the sequences of the two strains (Y-axis: 0-160 SNPs/kb). Gaps between contigs and centromeres are not to scale. The alignment demonstrates almost complete synteny between the two strains, with the exception of a cross-over event between the left arms of Chr III and VII.

7.1.3 Single nucleotide polymorphism analysis

In a comparison of single nucleotide polymorphisms (SNPs) between *A. niger* ATCC 1015 to *A. niger* CBS 513.88, 7.84±16.2 SNPs/kb (average±standard deviation) are found and a maximum of 163 SNPs/kb. In an analysis of the coding sequences (CDSs), the number of SNPs

per kb (6.71±14.5 SNPs/kb) was found to be less than the average for the chromosome, whereas promoter regions (1 kb upstream of the start codon) had more SNPs/kb than the average, and a similar variation (8.84±16.1 SNPs/kb). This is an expected result given that promoters are mostly non-coding regions with few functional motifs.

The large standard deviations suggest that the polymorphisms are not uniformly distributed, but clustered in hyper-variable regions. Mapping of the SNPs to the chromosomes confirms this (Figure 7.1).

Compared to a SNP-analysis done for two *F. graminearum* strains (Cuomo et al., 2007), where the authors found a maximum of 9 SNPs/kb, the values found here seem high. To estimate whether this is a typical level of variance for two *A. niger strains*, the genome sequence of *A. niger* ATCC 1015 was compared to that of *A. niger* ATCC 9029, and found significantly less variation (1.91±5.37 SNPs/kb). A graphical mapping of the SNPs of ATCC 9029 relative to ATCC 1015 (App. Figure E.2), shows that the variation between these strains is lower and more evenly distributed, and the hyper-variable regions do not coincide with those between *A. niger* ATCC 9029 and *A. niger* CBS 513.88.

7.1.4 Phylogenetic analysis

To further explore the genome variability across the *A. niger* species, regions of 1 kbp were selected from four chromosomes (II, IV, VI, VIII). These regions are identical in the ATCC 1015 and ATCC 9029 strains, but have approximately 20 SNPs/kb in a comparison to the CBS 513.88 genome sequence. Suitable primers were found in the regions, and the four regions were sequenced in six *A. niger* strains, including the CBS 513.88 progenitor, CBS 115989 and the *A. niger* neotype strain CBS 554.65 (Kozakiewicz et al., 1992), and CBS 126.49, earlier characterized to be *A. carbonarius* (Samson et al., 2004).

For the strains that are already sequenced, the re-sequencing was 100 % identical to the original genomic sequence, thereby excluding the possibility that the observed variation was erroneous, resulting from low-fidelity sequencing. Based on the combined sequences of the four regions, a phylogenetic tree was calculated (Figure 7.2).

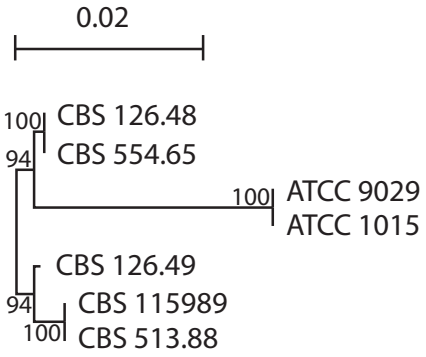

Figure 7.2: Phylogenetic relationship of seven strains of *A. niger*. The tree was rooted to the internode shown to comply with the exometabolomic clusters of Table 7.3.

The phylogenetic tree shows that CBS 513.88 and the progenitor strain CBS 115989 are clustering tightly in a clade (the sequences were checked to be identical), making it unlikely that the difference between the sequenced strains CBS 513.88 and ATCC 1015 are not due to strain improvement techniques such as UV mutagenesis. Also found in this clade is CBS 126.49, earlier characterized to be *A. carbonarius* (Samson et al., 2004). Interestingly, the *A. niger* neotype (CBS 554.65) is in a group that is distinct from both CBS 513.88 and ATCC 1015.

7.1.5 Examination of codon variation

The predicted CDSs from the genome sequences of *A. niger* ATCC 1015 and CBS 513.88 were compared based on codon preferences to examine whether the overall codon bias is different in the protein producer than in the acidogenic strain or there is reason to believe that the gene predictions in one strain contains a larger percentage of wrong gene calls than the other.

Figure 7.3 indicates several systemic differences between the codon usage in the two strains. Most noteworthy is the observation that all of the 10th percentiles of *A. niger* CBS 513.88

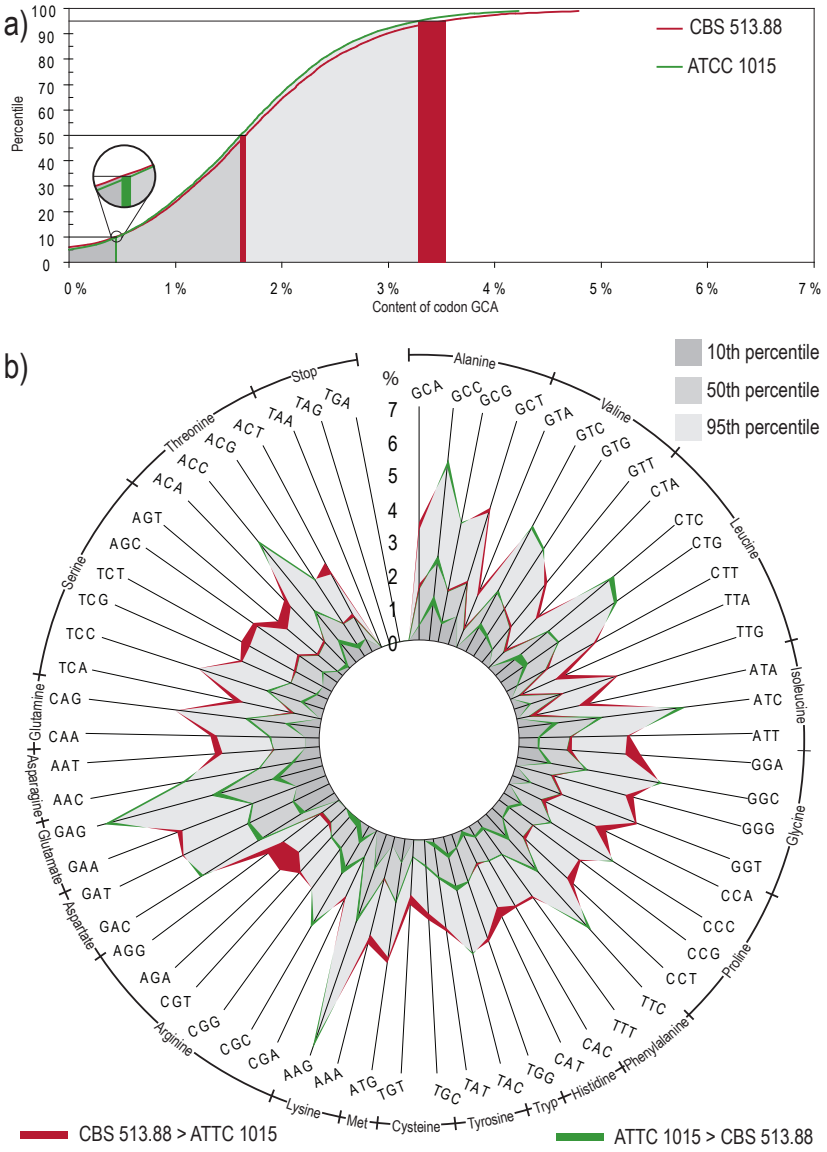

Figure 7.3: a): Cumulative distribution of codon GCA across the genes of *A. niger* strains ATCC 1015 and CBS 513.88. The nth percentile of a codon is defined as the percentage value, where n percent of the predicted genes have that percentage value or less of the given codon. The 100th percentile is not included, as this often represents a single outlier, and is thus not representative of the overall distribution. Vertical bars denote the differences between the values of the two strains. Red bars indicate that the higher value represents CBS 513.88, green shows higher values for ATCC 1015. b): Radar plot of the codon usage patterns for *A. niger* strains ATCC 1015 and CBS 513.88. Each colored band shows a percentile. If the band is red, the percentile of *A. niger* CBS 513.88 follows the outer rim of the band, while the percentile of ATCC 1015 follows the inner rim. A green band indicates the opposite.

are lower than those of *A. niger* ATCC 1015. *A. niger* CBS 513.88 for 42 of the 64 codons. Additionally, the 95th percentiles are higher for These two observations suggest that *A. niger*

CBS 513.88 has less specificity in codon usage than ATCC 1015.

To determine whether this observed effect was due to a higher percentage of erroneous gene calls or pseudo-genes in *A. niger* CBS 513.88 (note that 2935 more genes are predicted in CBS 513.88 (Table 7.1), the analysis was repeated with a subset of 9901 genes (Available from `www.computationalbiology.dk`) that are found in both gene sets using bi-directional best blastp hits (App. Figure E.3). In this plot, the percentiles are almost identical, and show that the codon variation in the common gene-set is slightly higher in ATCC 1015 than CBS 513.88. This means that the remaining genes not included in the second analysis greatly skews the variation towards higher codon variation in CBS 513.88. Based on this, the codons of these predicted genes must be under less selective pressure, making it likely that they are pseudogenes or artefacts of gene-calling. This was confirmed by a tblastn comparison of the predicted proteins of *A. niger* CBS 513.88 and ATCC 1015 and three other *Aspergillus* species, where a lower percentage of the predicted proteins of *A. niger* CBS 513.88 are shown to be conserved in the other Aspergilli than those predicted in ATCC 1015 (App. Figure E.4).

7.1.6 A novel method of gene model comparison

To compare the coding sequences of the two strains without the bias of different gene calling methods, the nucleotide sequence from *A. niger* CBS 513.88 corresponding to the gene set of *A. niger* ATCC 1015 was found using a novel method based on blastn (Imprint). This method provided detailed information on the differences in nucleic acid sequences for the predicted genes of the two strains, and allowed a categorization of the genes. The comparison found that 71 % of the genes differ on the nucleotide level and 56 % of the genes have non-silent mutations. A summary is found in Table 7.2 (The detailed table is available from `www.computationalbiology.dk`).

A GO term over-representation analysis of categories A–L of Table 7.2 revealed a surprising number of significant GO terms (Summary in Table 7.2, details in Appendix E.1). One observation was that ribosomal components are significantly over-represented (p=1.0e-21) in categories A and B (Appendix E.1.3). These two categories include a number of highly conserved cellular components such as the nucleosome, translation machinery, nucleosome and ribosome assembly machinery, and tRNA ligases. Also interesting is that proteins involved in regulation of transcription are over-represented in group I (Appendix E.1.20), suggesting that CBS 513.88 has fewer regulatory proteins than ATCC 1015.

To examine metabolic differences between the two strains, the gene comparison was reviewed using the ReMapper (chapter 4). All genes with amino acid level differences in the two strains were compared to the metabolic network and mapped to metabolic pathways (Appendix E.2). Several pathways relevant for protein production differ between the two strains. All genes of the biosynthetic pathways for proline, aspartate and asparagine differ between the strains. The genes of the entire tryptophan biosynthesis pathway in the two strains differ on the amino acid level with the exception of anthranilate phosphoribosyl transferase (EC 2.4.2.18) and two isoenzymes of 3-deoxy-7-phosphoheptulonate synthetase (EC 2.5.1.54). Four out of nine steps of histidine biosynthesis have mutations. Interestingly, a lot of variation is also found in the enzymatic machinery associated with citrate production: All steps of the electron transport chain have one or more components that differ between the strains, the extracellular proton pump is mutated, and the GABA shunt and enzymes around citrate in the tricarboxylic acid cycle differ between the two strains. Many of these traits were discussed in chapter 3 to be essential for citrate production. Additionally, several other pathways show ubiquitous variation: All steps of fatty acid synthesis and degradation have some isoenzymes that are differing, 12 in 22 genes of the sterol biosynthesis differ, and all steps of the pyrimidine biosynthetic pathway leading from glutamine to UMP are affected, with the exception of orotate phosphoribosyl transferase.

Examination of the annotation of the 3661

Table 7.2: Summary of the Imprint comparison of *A. niger* ATCC 1015 predicted genes to CBS 513.88 nucleotide sequence. A comprehensive listing with mapping of mutations, insertions, deletions and blast hit locations is presented is available from `www.computationalbiology.dk`. The 11,200 genes are divided into non-overlapping categories. Summaries of a GO term over-representation analysis for all categories and two lumped categories are found in the three right-most columns. For each of the three ontology types metabolic function (MF), cellular component (CC) and biological process (BP), the number of significantly over-represented GO terms are listed (Details in Appendix E.1).

Genes	Category	Description	MF	CC	BP
3288	A	Perfectly identical nucleotide sequences.	71	18	57
1627	B	Perfectly identical protein sequence, but with silent mutations.	22	11	39
	A+B	A and B combined	122	26	80
1375	E025	0–0.25 % sense mutations	118	4	30
1249	E050	0.25–0.50 % sense mutations	27	0	21
630	E075	0.50–0.75 % sense mutations	11	3	15
378	E1	0.75–1.00 % are sense mutations.	27	1	11
674	E2	1–2 % sense mutations.	71	3	15
316	E3	2–3 % sense mutations.	37	2	9
153	E4	3–4 % sense mutations.	34	2	6
82	E5	4–5 % sense mutations.	16	5	6
50	E6	5–6 % sense mutations.	11	5	3
25	E7	6–7 % sense mutations.	16	3	1
10	E8	7–8 % sense mutations.	8	2	1
9	E9	8–9 % sense mutations.	2	2	1
10	E10	9–10 % sense mutations.	1	2	0
	E5-10	E5-E10 combined	32	7	6
43	F	>10 % sense mutations.	4	4	5
40	G	20 or more of the bases could not find hits in CBS 513.88	12	0	6
691	I	Stop Codon or frame shift in the first 90 % of the gene	17	1	24
510	J	No hit	24	4	6
36	K	Stop codon to coding sequence in the first 90 % of the gene	6	4	3
4	L	>90 % of the gene is found on several contigs (Duplication)	2	0	1

genes of categories E075 through I of Table 7.2 revealed a number of interesting single genes with notable variability. Hypothetical components of the electron transport chain (one NADH ubiquinone oxidoreductase, an alternative oxidase and several NADH oxidases) were found in the groups having 0.75–2 % amino acid variation between the two strains. Three known extracellular glycoside hydrolases (*pgxA*, *aglA*, and *pgaI*) were found to have 2–3 % variation. Putative fungal transcription factors are present in most groups, but as many as 38 genes have non-sense codons or frame shift mutations in CBS 513.88 (category I). Among these are the cross-pathway control protein CpcA and the global repressor of nitrogen metabolism AreA, which has three separate single base deletions resulting in a stop codon in the segment that encodes the DNA binding domain in *A. nidulans* (Wilson and Arst Jr, 1998). However, PCR-based re-sequencing of the *areA* locus in strain CBS 513.88 revealed this to be a sequencing error in the CBS 513.88 sequence (data not shown). Even so, a comparative study of shake-flask cultivations showed that nitrogen source utilization is somewhat impaired in the CBS 513.88 strain (data not shown), suggesting mutations in downstream regulatory elements.

The group of ATCC 1015 predicted genes with no counterpart in the CBS 513.88 genome assembly (category J) includes 22 genes where the automatic annotation suggests regulatory ef-

fect on transcription as well as two predicted NADH:flavin oxidoreductases and one predicted NADH-ubiquinone dehydrogenase. The group of genes with a stop codon in ATCC 1015 restored to coding sequence in CBS 513.88 (category K) contains two proteins with putative transcriptional regulatory function. The four genes with putative duplications (category L) were confirmed not to be artefacts by manual examination of the nucleotide sequence, and are indeed two sets of very similar genes that suggest a duplication before the branching of the strains.

7.1.7 Exo-metabolome profiling

To compare the two sequenced strains to each other on a system-wide, but non-genomic level, exo-metabolomic profiles of the two strains were compared to nine other strains, including the CBS 513.88 progenitor strain NRRL 3122, the much applied and sequenced lab-strain ATCC 9029, and the *A. niger* neotype CBS 554.65 (Table 7.3).

CBS 513.88 produced aurasperone B, fumonisin B_2, nigragillin, ochratoxin A, pyranonigrin A and tensidol B and was very similar to the profile of secondary metabolites produced by the strain CBS 115989. These two strains differed quite significantly from the other strains analyzed. Strain ATCC 1015 and the strains related directly to it (NRRL 328, NRRL 350, NRRL 511, NRRL 1278 and NRRL 2270), did not produce ochratoxin A or nigragillin, but they all produced funalenone, kotanin, and orlandin in addition to the secondary metabolites common for all strains (fumonisin B_2, pyranonigrin A, tensidol B, aurasperone B). ATCC 9029 and CBS 554.65, the *A. niger* neotype, produced the same metabolites as ATCC 1015, although there were some quantitative differences.

7.1.8 Characterization and transcription analysis of batch cultures

In order to evaluate the effect of the differences in genome sequence on the physiology of the two strains, a comparative transcriptome analysis was performed. The two strains were grown under exactly the same conditions in batch cultures in a glucose-based minimal medium designed for enzyme production and dispersed filamentous growth. Samples were harvested for transcriptome and metabolite analysis. The transcriptome was profiled using an Affymetrix array based on the genome sequence of ATCC 1015 (Andersen et al., 2008b). Several characteristics of the culture physiologies were measures and are shown in Table 7.4. Glucoamylase A activity levels were measured to be more than six times higher in cultivations of the glucoamylase A-producing strain *A. niger* CBS 513.88 than in ATCC 1015.

Table 7.4: Statistics for batch cultivations of *A. niger* ATCC 1015 and *A. niger* CBS 513.88. Fermentations were performed in biological triplicates for each strain. Values are presented as average±standard deviation. μ_{max} and Y_{xs} are general statistics for the fermentations, while the remaining values are specific for the time of mRNA sampling for transcription analysis (The mRNA column). GlaA is glucoamylase A.

	ATCC 1015	CBS 513.88
mRNA (h)	24.5±1.15	40.19±4.2
Biomass (g/L)	4.98±0.07	4±0.49
$\mu_{\max}$ (h^{-1})	0.17±0.004	0.15±0.01
Glucose (g/L)	9.95±0.58	9.51±0.44
Glycerol (g/L)	0.09±0.02	0.27±0.03
Citric acid (g/L)	0.10±0.12	0.14±0.03
Y_{xs} (Cmol/Cmol)[1]	0.67±0.03	0.55±0.03
GlaA (U/mL)[2]	9.58±3.22	62.76±9.25

[1]Biomass was converted to Cmol by the factor 24.9 g biomass/Cmol (Nielsen et al., 2003b)

[2]One unit of glucoamylase can be assumed to correspond to 25μg of protein (PESL protein assay; Boehringer Mannheim, Mannheim, Germany).

Statistical analysis showed 4784 significantly differentially expressed genes, 2431 of them having a higher expression index in *A. niger* CBS 513.88 and 2353 a higher index in *A. niger* ATCC 1015.

To further explore the differences in metabolism of the two strains, the significantly differentially expressed genes were examined in context of the metabolic network

Table 7.3: Exo-metabolomic profiling of 11 *A. niger* strains

Secondary metabolites	Reference	CBS 115989	CBS 513.88[a]	CBS 126.49	ATCC 1015[a]	ATCC 9029[a]	CBS 554.65	NRRL 328	NRRL 350	NRRL 511	NRRL 1278	NRRL 2270
Aurasperone B	(Tanaka et al., 1966)	•	•	•	•	•	•	•	•	•	•	•
Fumonisin B_2	(Frisvad et al., 2007)	•	•		•	•	•	•	•	•	•	•
Funalenone	(Inokoshi et al., 1999)			•	•	•	•	•	•	•	•	•
Kotanin	(Büchi et al., 1971)			•	•	•	•	•	•	•	•	•
Nigragillin	(Isogai et al., 1975)	•	•									
Ochratoxin A	(Abarca et al., 1994)	•	•	•								
Orlandin	(Cutler et al., 1979)			•	•	•	•	•	•	•	•	•
Other naphtho-γ-pyrones				•	•	•	•	•	•	•	•	•
Pyranonigrin A	(Hiort et al., 2004)	•	•	•	•	•	•	•	•	•	•	•
Tensidol B	(Fukuda et al., 2006)	•	•	•	•	•	•	•	•	•	•	•

[a] Sequenced strains

(Appendix E.3). A substantial overweight of the metabolic genes were up-regulated in CBS 513.88, including central pathways such as glycolysis and the tricarboxylic acid cycle. This was rather surprising, as an almost equal number of genes were up-regulated in each of the two strains, and the specific maximum growth rate of ATCC 1015 is the higher of the two, which should logically give higher expression levels of genes involved in the production of precursors for biomass and replication machinery, but this seems not to be the case. Thus, a higher production of extracellular enzyme and a different mode of growth can produce an effect that is at least equal to that of a higher growth rate.

When examining the figure of Appendix E.3 for entire pathways up-regulated in either strain, the biosynthetic pathways of threonine, serine, lysine and tryptophan were found to be up-regulated in CBS 513.88. Intriguingly, a codon usage analysis (Figure 7.4) of the glucoamylase A gene (*glaA*) revealed that *glaA* is atypical in that it has a higher percentage of tryptophan codons than 90 % of all the predicted genes of *A. niger* CBS 513.88, and twice as high a tryptophan content as the average in the biomass composition measured by Christias et al. (1975). As many mutations were found in the biosynthetic pathway of tryptophan as well, this was a surprising coincidence. Additionally, threonine and serine codons also have high levels in *glaA*. The combination of these results suggests that high-yield production of enzymes is highly dependent on corresponding increased production of amino acids that are over-represented in the product.

Other pathways generally up-regulated in CBS 513.88 include purine and pyrimidine biosynthesis and chitin biosynthesis. Very few metabolic pathways are generally up-regulated in ATCC 1015, but the few that are include most of the sterol biosynthesis pathway and the alternative oxidative pathway.

To identify significant trends in the transcriptome profile of the two strains, a GO term over-representation analysis was conducted on the genes up-regulated in either strain. The analysis showed that genes up-regulated in CBS 513.88 have a number of significant traits relevant to high yield protein production, specifically amino acid biosynthesis and tRNA aminoacylation activities. The same GO term over-representation study of ATCC 1015 did not propose terms of a similar trend, however, electron transport was the most significantly over-represented biological process GO term (Tables 7.6 and 7.5, details in Appendix E.4). Individual examination of the regulated genes showed the presence of an alternative oxidase and the mitochondrial proton gradient driven ATPase. These were described in Figure 3.5 to be essential for high-yield citrate production. An up-regulation of genes annotated

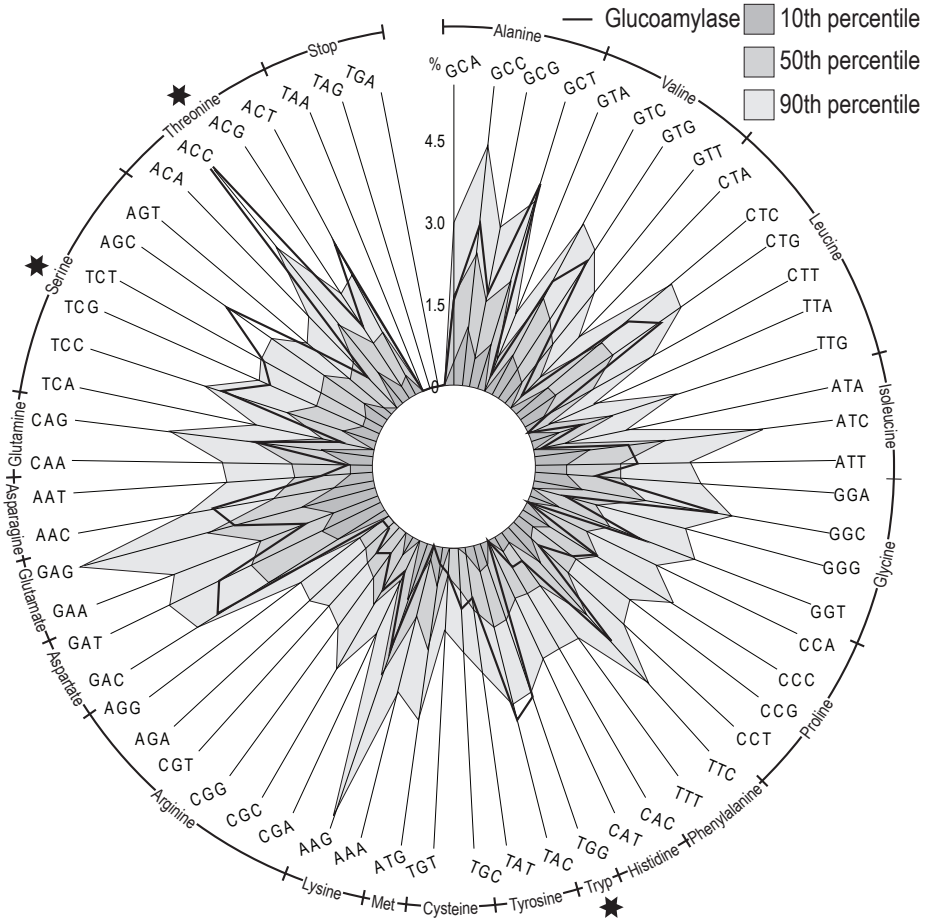

Figure 7.4: Radar plot of the codon usage of *A. niger* CBS 513.88 and glucoamylase A (*glaA*) coding region. Three percentiles are shown as colored areas. The nth percentile of a codon is defined as the value, where n percent of the genes have less than that percentage of the given codon. The codon distribution of *glaA* is shown as well (black line). *glaA* has a particularly high content of tryptophan, threonine and serine codons (Marked with stars).

to have functions in carbohydrate transport and transport of organic acids are seen as well.

An examination of the individual regulated genes to find single genes of special interest, showed that regulation of glucoamylase A was significantly up-regulated in CBS 513.88 (adj.p = 84e-6), but the fold change is merely 3.2 compared to the more than 6-fold higher glucoamylase activity of these cultivations. Additionally, all identified tRNA-aminoacyl synthases were found to be two- to six-fold up-regulated in CBS 513.88 (Table 7.4). An up-regulation of a candidate urea decarboxylase in CBS 513.88 is also seen, which adds to the likelihood of a deregulated nitrogen metabolism, since no urea was present in the medium.

7.1.9 Mapping of gene expression to the genome

To examine differences in gene expression between the two strains relative to chromosome positions, the log2-ratios of the gene expression indices from the transcriptome analysis were mapped to the synteny maps (Figure 7.5). This allows the identification of chromosome regions

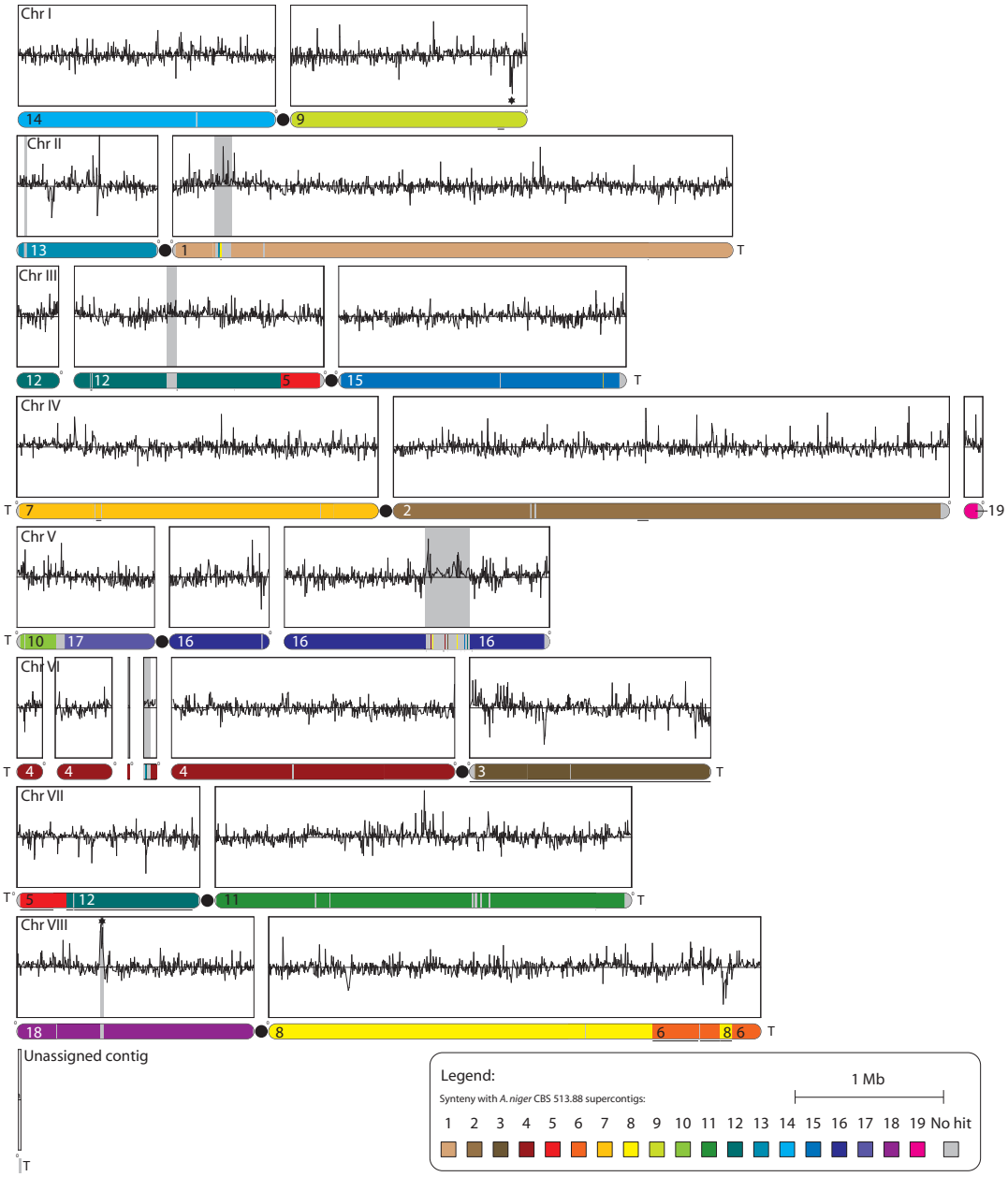

Figure 7.5: Mapping of gene log2-ratios to a synteny map of the contigs of A. niger ATCC 1015 to the supercontigs of A. niger CBS 513.88. The coloring of the chromosomes is the same as in Figure 7.1 and shows syntenic regions in A. niger CBS 513.88. Arabic numerals show the number of the supercontig in A. niger CBS 513.88. The graphs above the chromosomes show the log2-ratio of the average expression index for each gene predicted in ATCC 1015. Log2-ratios are mapped to the position of the first base of the gene. The scale of the Y-axis is from -9 to 9, with higher expression index in ATCC 1015 being the positive values (above the line). Gray areas show regions that are not found in the genome sequence of CBS 513.88 and the genes all have higher expression indices in ATCC 1015 (log2 > 0). Stars mark putative secondary metabolite clusters with uniformly higher expression levels in one strain versus the other.

with a uniformly higher expression in one of the strains.

The parts of the genome assembly of ATCC 1015 that do not find hits in the CBS 513.88 sequence are of special interest, since uniformly higher expression in ATCC 1015 of all genes in the entire region suggests that this region is not present in ATCC 1015. This is seen to be the case for six large regions, including the largest area in the genome not found in CBS 513.88 (Figure 7.5). If all of these regions are indeed absent from the genome of CBS 513.88, this explains a proportion of the reported difference in genome size (Table 7.1).

Two putative secondary metabolite clusters have high log2-ratios. One is the region in chromosome VIII not found in CBS 513.88, the other is a cluster on the right arm of chromosome I, close to the centromeric region that is greatly up-regulated in CBS 513.88. The elevated cluster on chromosome VIII includes a putative polyketide synthase (Gene ID: 211885), that is nearly identical to an *A. fumigatus* gene (AFUA_1G17740). The cluster on chromosome I contains a putative non-ribosomal peptide synthase (NRPS) (Gene ID: 43555) with a transcription factor (Gene ID: 188323). These clusters should be initial targets for a survey of the genetic background of the differences in exo-metabolomic profiles (Table 7.3).

Additionally, the transcriptome mapping confirms the inversion of the entire right arm of chromosome VI that was discussed in the section on synteny (Figure 7.1). A telomeric position effect — the proximity of a gene to the telomeric end reduces expression — has been described for *S. cerevisiae* by Gottschling et al. (1990), and applied for the orientation of chromosome arms in *A. niger* CBS 513.88 (Pel et al., 2007). Thus, if an arm has been inverted, reduced expression should be found at opposite ends in ATCC 1015 and CBS 513.88, thereby influencing the log2 ratio. This is indeed seen on the right arm of chromosome VI with the numerical log2-ratios increasing towards the two ends.

7.2 Discussion

The nearly gap-less *A. niger* ATCC 1015 genome assembly is the most comprehensive *A. niger* genome sequence to date and has allowed the expansion of our knowledge of genomic variation within the *A. niger* species. While the genomes of *A. niger* ATCC 1015 and *A. niger* CBS 513.88 are largely syntenic, a detailed examination of the single nucleotide polymorphisms (SNPs) showed a surprisingly high variation between the strains, and a noticeably lower difference between *A. niger* ATCC 1015 and *A. niger* ATCC 9029. Several possible theories can be proposed for this: 1) A larger percentage of sequencing errors in the *A. niger* CBS 513.88 genome data, as this was sequenced less recently and therefore with older techniques. 2) The variation is caused by mutagenesis in the pedigree of the industrial CBS 513.88 strain. 3) A sub-speciation or a mis-classification of one or more of the strains. While distantly related Aspergilli have lower degrees of synteny, as seen in the published analysis of the genome of *A. nidulans* (Galagan et al., 2005) and *A. niger* CBS 513.88 (Pel et al., 2007), closely related species may be as similar as these two strains. 4) Previously un-described high genetic variation within the *A. niger* species.

To examine these four possibilities, regions with moderate (2 %) variation between the two species were re-sequenced in seven strains (Figure 7.2). Across 75 re-sequenced SNPs, none of them were sequencing errors, which excludes the possibility that low-fidelity sequencing in either genome sequence is the sole reason for the variation between the genomes (theory 1 above). The complete identity of the sequence from strains CBS 115989 and 513.88 exclude the possibility that the variation is caused by mutagenesis (theory 2), but the strains do form a separate clade with *A. carbonarius* CBS 126.49, which suggests theory 3 — sub-speciation or a mis-classification of CBS 513.88/115989 — to be true. If this is not the case, then the *A. niger* species holds high variation on the genetic level, and the relation between isolates ATCC 1015 and CBS 513.88 is indicative of the maximum level of variation in the *A. niger* species.

The examination of the exo-metabolomic pro-

Table 7.5: GO term over-representation of the 1000 most up-regulated significantly differentially expressed genes in cultivations of *A. niger* CBS 513.88. The top ten terms of the GO ontology Biological Processes are shown. See Appendix E.4 for more details.

#	GO.ID	Term	Annotated	Significant	Expected
1	GO:0006418	tRNA aminoacylation for protein translation	50	21	5.38
2	GO:0006526	Arginine biosynthetic process	8	6	0.86
3	GO:0009082	Branched chain family amino acid anabolism	12	7	1.29
4	GO:0007049	Cell cycle	34	12	3.66
5	GO:0000059	Protein import into nucleus, docking	10	6	1.08
6	GO:0009073	Aromatic amino acid family biosynthetic process	19	8	2.04
7	GO:0016043	Cell organization and biogenesis	220	43	23.67
8	GO:0009067	Aspartate family amino acid biosynthetic process	9	5	0.97
9	GO:0050658	RNA transport	3	3	0.32
10	GO:0015031	Protein transport	107	26	11.51

Table 7.6: GO term over-representation of all significantly differentially expressed genes up-regulated in cultivations of *A. niger* ATCC 1015. The top ten terms of the GO ontology Biological Processes are shown. See Appendix E.4 for more details.

#	GO.ID	Term	Annotated	Significant	Expected
1	GO:0006118	Electron transport	599	153	115.07
2	GO:0006564	L-serine biosynthetic process	18	10	3.46
3	GO:0051341	Regulation of oxidoreductase activity	34	15	6.53
4	GO:0008643	Carbohydrate transport	101	30	19.4
5	GO:0009410	Response to xenobiotic stimulus	22	9	4.23
6	GO:0042221	Response to chemical stimulus	99	27	19.02
7	GO:0006865	Amino acid transport	87	24	16.71
8	GO:0015837	Amine transport	87	24	16.71
9	GO:0015849	Organic acid transport	87	24	16.71
10	GO:0046942	Carboxylic acid transport	87	24	16.71

files of the strains of the phylogenetic comparison and four more for diversity (Table 7.3) indicated three distinct groups of produced exo-metabolites: CBS 513.88 has a distinct metabolite profile similar to its progenitor strain CBS 115989, strains ATCC 1015 and ATCC 9029 are similar to the neotype, and finally CBS 126.49, the strain closest related to CBS 513.88 and its progenitor in the phylogenetic tree (Figure 7.2), has a profile somewhere between the two groups. The grouping of CBS 513.88 and CBS 115989 further confirms that the exo-metabolite profile is not caused by strain improvement programs involving mutagenesis.

Based on the exo-metabolome results of Table 7.3, it is possible that CBS 513.88/CBS 115989 represents a distinct species, while ATCC 1015 and ATCC 9029 groups with the neotype, making them typical *A. niger* in this respect. The most closely related species to *A. niger*, *A. tubingensis*, differs from *A. niger* in producing asperazine and not being able to produce fumonisins, ochratoxins and kotanins (Samson et al., 2004, 2007), meaning that association with this species is unlikely. However it is possible that the genes for ochratoxin A production are silent in the ATCC 1015/ATCC 9029 group and for funaleone and kotanin in the group containing CBS 513.88 and NRRL 3122. In that case, all the strains considered here belong to the same species.

The Imprint-based comparison of the genes predicted in the genome sequence of strain ATCC 1015 has illustrated many nucleotide-level differences differences between the citric-acid producing *A. niger* ATCC 1015 and the glucoamylase producing CBS 513.88, as well as producing a catalogue of genetic alleles in the 6285 predicted genes with differences in amino acid

sequence. The differences in metabolic pathways relevant to citric acid production or protein synthesis are especially interesting, particularly the electron transport chain and the biosynthesis of tryptophan.

Characteristic of the transcriptome analysis is that an overlap is found between pathways that have mutations in most of the genes, and pathways with significant regulation. Examples of this can be found for the sterol pathway, tryptophan biosynthesis, and the alternative oxidase pathway. This is especially the case for the investigations of glucoamylase production. It seems evident that the high-yielding strain is the result of changes in multiple related pathways and at several levels, also indicated by the fact that increase in glucoamylase activity (Table 7.4) is twice as big as the difference in transcription level. Mutations in relevant genes, induction of the transcription of the genes of amino acids biosynthesis pathways, especially tryptophan biosynthesis that is a likely bottleneck, and general up-regulation of tRNA-synthases all contribute.

A consequence of the high level of SNPs/kb, is that it may affect transcriptome analysis. Since the microarray employed for the transcriptional analysis was designed from the coding sequences of *A. niger* ATCC 1015, the probability of mismatching probes is higher for the *A. niger* CBS 513.88 strain. This may lead to an underestimation of the transcriptional levels in this strain. The use of the medianpolish algorithm (Irizarry et al., 2003) makes the calculations of gene expression indexes relatively robust to this effect. Genes found to be overexpressed in the *A. niger* CBS 513.88 can surely be trusted, but caution should be exerted when examining genes only slightly overexpressed in *A. niger* ATCC 1015. In light of the results, it seems important that in comparative transcriptomic studies, one should — if available — use a microarray designed for the strain closer related to the background strain of ones study.

Another fact that should be considered in molecular biology or metabolic engineering studies of *A. niger*, is that successful PCR primer design may be dependent on choosing the correct genome sequence. In the phylogenetic study, regions initially planned to be included were rejected since it was not possible to design primers that could amplify the region in both strains, even with slightly degenerated primers.

7.3 Conclusion

The sequencing of *A. niger* ATCC 1015 has produced a high-quality fungal genome sequence. Assuming correct assembly, the sequence covers almost the entire genome. The high fidelity of this allows for detailed studies of synteny across the *Aspergillus* genus, and can catalyze the gap-closure finishing of the estimated remaining 1 Mb of sequence of *A. niger* CBS 513.88, thereby producing two fully sequenced strains. Since *A. niger* CBS 513.88 differs from ATCC 1015 in terms of genome sequence, chromosome configuration and exo-metabolome profile, and ATCC 1015 has more similarities with the lab-strain ATCC 9029 and the *A. niger* neotype, the possibility of CBS 513.88 being a separate species or belonging to a sub-species cannot be excluded. A future whole-genome sequencing of *A. carbonarius* (as mentioned in chapter 2) will hopefully cast further light on the phylogeny of the black Aspergilli.

Even so, the relationship between the two species cannot be denied, and much can be learned by comparing them at a genetic level as well as system-wide. For gene-to-gene comparisons, the presented results from the analysis with the Imprint algorithm provides a comprehensive overview of the differences and similarities of the genes of the two strains. For further studies in single genes and pathways, this is a powerful resource of many applications.

Finally, much information has been generated through the genomic and transcriptomic profiling of the strains, and it is clear that specialization as an acidogenic or an enzyme-producing strain involves customization on multiple levels. Especially the information presented on over-representation of codons in a high-yield protein and the corresponding up-regulation of bio-synthetic pathways and tRNA-aminoacyl synthases can aid the construction of improved industrial strains through metabolic engineering

strategies.

7.4 Methods

7.4.1 Genome assembly

The sequence reads were derived from four whole-genome shotgun (WGS) libraries: One with an insert size of 2–3 kbp, two with an insert size of 6–8 kbp, and one with an insert size of 35–40 kbp. The reads were screened for vector using cross_match, then trimmed for vector sequence and quality (Chapman et al., Unpublished). Reads shorter than 100 bases after trimming were excluded. The final data set included: 28,551 2–3 kb reads, containing 21.5 Mb of sequence, 160,479 6–8 kb reads, containing 123 Mb of sequence, and 38,651 35–40 kb reads, containing 23.8 Mb of sequence.

The data was assembled using release 2.7 of Jazz, a WGS assembler developed at the JGI (Aparicio et al., 2002, Chapman et al., Unpublished). The genome size and sequence depth were initially estimated to be 36 Mb and 8.0, respectively. After removal of short (less than 1 kb) and redundant scaffolds (shorter than 5 kb with 80 % or more of the length matching a scaffold longer than 5 kb), the assembly included 43.7 Mb of scaffold sequence with 8.2 Mb (18.9 %) of gaps in 350 scaffolds, with half of the scaffold sequence contained in the eight largest scaffolds of 1.81 Mb or longer. The sequence depth derived from the assembly was 7.88 $\pm$ 0.05. To estimate the completeness of the assembly, a set of 50,001 ESTs was BLAT-aligned to the unassembled trimmed reads, as well as the assembly itself. 43,323 ESTs (86.6 %) were more than 80 % covered by the unassembled data, 43,978 (88.0 %) were more than 50 % covered, and 44,206 (88.4 %) were more than 20 % covered. By way of comparison, 48,798 ESTs (97.6 %) had hits to the assembly.

7.4.2 Automatic annotation

Gene models in the genome of *A. niger* were predicted using Fgenesh (Salamov and Solovyev, 2000), Fgenesh+ (Salamov and Solovyev, 2000), and Genewise (Birney and Durbin, 2000) integrated in the JGI annotation pipeline. Fgenesh was trained on a set of over 2000 putative full-length transcripts derived from clustered *A. niger* ESTs and reliable homology-based gene models to show 81 % sensitivity and 81 % specificity of predictions on a test set. Homology based gene predictors were seeded with blastx alignments of proteins from the NCBI non-redundant set of proteins. 31,578 *A. niger* ESTs were sequenced using Sanger technology and were either directly mapped to genomic sequence when the ESTs included putative full-length (FL) genes, or used to extend predicted gene models into FL genes by adding 5' and/or 3' untranslated regions (UTRs). In addition, 386,515 ESTs with an average length of 104 nucleotides were sequenced with 454 GS20 sequencers and used in validation of predicted gene models. Since multiple gene models were generated for each locus, a single representative model was chosen based on homology and EST support and used for further analysis.

All predicted gene models were functionally annotated by sequence similarity to annotated genes from the NCBI non-redundant set and other specialized databases (like KEGG (Kanehisa et al., 2004, 2002)) using Blast and hardware accelerated double-affine Smith-Waterman alignments (`www.timelogic.com`). Functional and structural domains were predicted in protein sequences using the InterPro software (Zdobnov and Apweiler, 2001). All genes were also annotated according to Gene Ontology, eukaryotic orthologous groups (KOGs (Koonin et al., 2004)), and KEGG metabolic pathways (Kanehisa et al., 2004).

7.4.3 Sequence availability

A. niger assemblies, annotations, and analyses are available through the interactive JGI Genome Portal at `http://genome.jgi-psf.org/Aspni1/Aspni1.home.html`. The finished version of the *A. niger* is available from Scott E. Baker upon request and will be made available through NCBI/GenBank upon publication of the sequence.

7.4.4 Strains

The following *A. niger* strains were used for experiments (deposition numbers in different collections are given as well):

- CBS 513.88 = IBT 29270
- ATCC 1015 = IBT 28639 = NCTC 3858a = NRRL 1278 = NRRL 350 = NRRL 511 = NRRL 328 = Thom 167 = CBS 113.46 = ATCC 10582 = IMI 031821 = LSBH Ac4 = Thom 3528.7
- NRRL 3 = IBT 28539 = MUCL 30480 = DSM 2466 = CECT 2088 = VTT D-85240 = NRRL 566 = WB3 = ATCC 9029 = N400 = CBS 120.49 = IMI 041876
- NRRL 326 = IBT 27876 = WB 326 = CBS 554.65 = ATCC 16888 = IHEM 3415 = IMI 050566 = Thom 2766 = JCM 10254 = IFO 33023 (ex tannin-gallic acid fermentation, Connecticut, USA) (*A. niger* neotype (Kozakiewicz et al., 1992))
- NRRL 328 = IBT 27878
- NRRL 337 = CBS 126.48 = ATCC 10254 = DSM 734 = IFO 6428 = IMI 015954 = WB 337
- NRRL 350 = IBT 27877
- NRRL 363 = IBT 3617 = IBT 5764 = CBS 126.49 = ATCC 10698 = IFO 6648
- NRRL 511 = IBT 27875
- NRRL 1278 = IBT 27872
- NRRL 2270 = IBT 26391 = ATCC 11414 = VTT D-77050 = IMI 075353 = A60 = S.M. martin A-1-233 = Wisconsin 72-4, derived from ATCC 1015
- NRRL 3122 = IBT 23538 = ATCC 22343 = CBS 115989 (This strain is a wild type progenitor of CBS 513.88).

7.4.5 Exo-metabolite profiling

A. niger strains were inoculated on Czapek yeast autolysate (CYA), yeast extract sucrose (YES) agar and CYA with 5 % NaCl agar (CYAS agar). For medium composition see Frisvad and Samson (2004). All strains were three point inoculated on these media and incubated at 25°C in darkness for a week, after which 5 plugs (6 mm diameter) along a diameter of a fungal colony were cut out and extracted (Smedsgaard, 1997). The extracts were analyzed by HPLC-DAD-fluorescence (Frisvad and Thrane, 1987, Smedsgaard, 1997) and by HPLC-HR-MS (Nielsen and Smedsgaard, 2003, Frisvad et al., 2007). The secondary metabolites were identified by comparison with authentic standards (fumonisin B_2, ochratoxin A, nigragillin, kotanin and orlandin were available) and by UV spectra and high resolution mass spectra using electrospray ionization.

7.4.6 Sequencing of variable regions

Regions were amplified using standard PCR techniques with the four following primer pairs: 1) Chr02-Fwd: 5'-GGACACTGCTTGATGTGATG-3', Chr02-Rev: 5'-GAGAGACGTACGAAAGGTTG-3'. 2) Chr04-Fwd: 5'-CGATCTGCGACCAGGA-3', Chr04-Rev: 5'-CATAACGGATTCGTCGCTG-3'. 3) Chr06-Fwd: 5'-CTTGAAGGCGTTGAGGTC-3', Chr06-Rev: 5'-GCGAGTATGTGGCTAACATC-3'. 4) Chr08-Fwd: 5'-GGTATGTCACATTCCRTCCA-3', Chr08-Rev: 5'-GCTTGCAGTGAGCAAGGA-3'. The name describes chromosome number and direction. The sequences on chromosomes II, VI, and VIII overlap with predicted genes. The PCR products were purified using a QIAquick PCR Purification Kit (Qiagen Inc, USA) and sequenced by Agencourt Bioscience Corporation (Beverly, Massachusetts).

7.4.7 Calculation of phylogenetic tree

For each of the four sets of seven sequences described above, the set was aligned using ClustalX and trimmed to first common base at both ends. The four trimmed sequences for

each strain were joined in numerical chromosome order to produce a 2665–2668 bp sequence for each. Tree calculations were done using TreeCon. Distances were estimated using the Jukes and Cantor algorithm taking insertions and deletions into account. Topology was inferred using neighbor joining with bootstrap-values based on 1000 reiterations.

7.4.8 Fermentation procedure

Growth media

A. niger batch cultivation medium: 20 g/L glucose monohydrate, 7.3 g/L $(NH_4)_2SO_4$, 1.5 g/L KH_2PO_4, 1.0 g/L $MgSO_4 \cdot 7H_2O$, 1 g/L NaCl, 0.1 g/L $CaCl_2$, 0.05 mL/L antifoam 204 (Sigma) and 1 mL/L trace element solution. Trace element solution composition: 7.2 g/L $ZnSO_4 \cdot 7H_2O$, 0.3 g/L $NiCl_2 \cdot 6H_2O$, 6.9 g/L $FeSO_4 \cdot 7H_2O$, 3.5 g/L $MnCl_2 \cdot 4H_2O$ and 1.3 g/L $CuSO_4 \cdot 5H_2O$. *A. niger* complex medium: 2 g/L yeast extract, 3 g/L tryptone, 10 g/L glucose monohydrate, 20 g/L agar, 0.52 g/L KCl, 0.52 g/L $MgSO_4 \cdot 7H_2O$, 1.52 g/L KH_2PO_4 and 1 mL/L of trace elements solution. Trace elements solution: 0.4 g/L $CuSO_4 \cdot 5H_2O$, 0.04 g/L $Na_2B_4O_7 \cdot 10H_2O$, 0.8 g/L $FeSO_4 \cdot 7H_2O$, 0.8 g/L $MnSO_4 \cdot H_2O$, 0.8 g/L $Na_2MoO_4 \cdot 2H_2O$, 8 g/L $ZnSO_4 \cdot 7H_2O$.

Spore propagation

The fermenters were inoculated with spores of *A. niger* CBS 513.88 or ATCC 1015 strains previously propagated on complex media plates and incubated for 8 days at 30°C. The same stock of spores was used to inoculate all the plates. Spores were harvested by adding 10 mL of Tween 80 0.01 %, centrifuged at 4000 rpm for 10 min and washed three times with a suitable amount of 0.9 % NaCl. The fermenters were inoculated with a spore suspension to obtain a final concentration of 5.7×10^9 spores L^{-1}.

Batch cultivations

A. niger batch cultivations were carried out in 5 L reactors with a working volume of 4.5 L. The bioreactors were equipped with two Rushton four-blade disc turbines, and pH and temperature control. Inlet air was controlled with a mass flowmeter. The concentrations of oxygen and carbon dioxide in the exhaust gas were monitored with a gas analyzer (1311 Fast response Triple gas, Innova combined with multiplexer controller for Gas Analysis MUX100, B. Braun Biotech International). The temperature was maintained at 30°C and the pH was controlled by automatic addition of 2 M NaOH. The pH was initially set to 3.0 to prevent spore aggregation; when spores started to germinate, the pH was gradually increased to 4.5. Similarly, the stirring speed was initially set to 200 rpm and the aeration rate to 0.05 vvm to prevent loss of hydrophobic spores from the medium to the head-space of the reactor. After germination, these parameters were progressively increased to 600 rpm and 0.89 vvm and kept steady throughout all the rest of the fermentation.

Sampling

For quantification of cell mass and extracellular metabolites, the fermentation broth was withdrawn from the reactor, filtered and washed. The filter cakes were used for cell weight determination. The filtrate was filtered once more and frozen at -20°C for HPLC analysis later.

For gene expression analysis, mycelium was harvested at the exponential phase by filtration through sterile Mira-Cloth (Calbiochem, San Diego, CA, USA) and washed with a suitable amount of 0.9 % NaCl solution. The mycelium was quickly dried by squeezing, and subsequently frozen in liquid nitrogen. Samples were stored at -80°C until used for RNA extraction.

Cell mass determination

Cell dry weight was determined using paper filters (Whatman cat. no. 1001070). The filters were pre-dried in an oven at 100°C for 24 h, cooled down in a desiccator for 2 h and subsequently weighed. A known volume of cell culture was filtered and the residue was washed with 0.9 % NaCl and dried on the filter for 24 h in an oven at 100°C. The filter was weighed again and the cell mass concentration was calculated.

Quantification of sugars and extracellular metabolites

The concentrations of sugar and organic acids in the filtrates were determined using HPLC on an Aminex HPX-87H ion-exclusion column (BioRad, Hercules, CA). The column was eluted at 60°C with 5 mM H_2SO_4 at a flow rate of 0.6 $^{mL}/_{min}$. Metabolites were detected with a refractive index detector and a UV detector.

Determination of glucoamylase activity

The activity of glucoamylase in culture filtrates was quantified spectrophotometrically using p-nitrophenyl β-maltoside as the substrate for glucoamylase. 90 μL of sodium acetate 200 mM (pH 4.4) were added to 10 μL of enzyme solution (standards or fermentation broth), mixed and shaken for 30 s in a microtiter plate, then incubated 5 min at 40°C. 10 μL of this mixture were taken and mixed with 10 μL of substrate containing p-nitrophenyl β-maltoside plus thermostable β-glucosidase. This preparation was shaken for 30 s and incubated for 10 min at 40°C. The reaction was stopped by the addition of 150 μL of trizma base solution 2 %. The sample preparation was shaken again for 30 seconds and measured at 405 nm wavelength in a spectrophotometer. The absorbance measurement was related to enzyme units per mL according to the calibration curve. 1 U of enzyme is the amount of enzyme which liberates 1 μmol of glucose per minute at pH 4.8 and 60°C.

7.4.9 Transcriptome analysis

Extraction of total RNA

Total RNA was isolated using the Qiagen RNeasy Mini Kit (Qiagen Nordic, Ballerup, Denmark), according to the protocol for isolation of total RNA from plant and fungi. For this purpose, 70–90 mg of frozen mycelium were placed in a 2 mL Eppendorf tube, pre-cooled in liquid nitrogen, containing three RNase-treated steel balls (two balls with a diameter of 2 mm and one ball with a diameter of 5 mm). The tubes were then shaken in a Mixer Mill, at 5°C for 10 minutes, until the mycelium was ground to powder, and thus ready for extraction of total RNA. The quality and the quantity of the total RNA extracted were determined with a BioAnalyzer (2100 BioAnalyzer, Agilent Technologies Inc., Santa Clara, CA, USA) and a spectrophotometer(Amersham Pharmacia Biotech, GE Healthcare Bio-Sciences AB, Uppsala, Sweden), respectively. The total RNA was stored at -80°C until further processing.

Preparation of biotin-labeled cRNA and microarray processing

20 μg of fragmented biotin-labeled cRNA was prepared from approximately 1 μg of total RNA according to the Affymetrix GeneChip Expression Analysis Technical Manual(Aff, 2007). The cRNA was cleaned before fragmentation using the Qiagen RNeasy Mini Kit (protocol for RNA Cleanup), in order to guarantee good-quality cRNA samples for subsequent processing. The biotin-labeled cRNA was quantified in a spectrophotometer (same as above) and subsequently fragmented. Approximately 15 μg of fragmented cRNA was hybridized to the 3AspergDTU GeneChip (Andersen et al., 2008b) following the Affymetrix GeneChip Expression Analysis protocol. The array was washed and stained using a GeneChip Fluidics Station FS-400, and scanned on an Agilent GeneArray Scanner 3000. The scanned probe array images (.DAT files) were converted into .CEL files using the Affymetrix GeneChip Operating Software.

Analysis of transcription data

Affymetrix CEL-data files were preprocessed using the statistical language and environment R (R Development Core Team, 2007) version 2.5. The probe intensities were normalized for background using the RMA method (Irizarry et al., 2003) using only perfect match (PM) probes. Normalization was performed subsequently using the quantiles algorithm (Bolstad et al., 2003). Gene expression values were calculated from the PM probes with the medianpolish summary method (Irizarry et al., 2003). All statistical preprocessing methods were used by invoking them through the affy package (Gautier et al., 2004).

Statistical analysis was applied to determine

genes subject to differential transcriptional regulation. The limma package (Smyth, 2004) was used to perform moderated t-tests between the two carbon sources for each of the three species. Empirical Bayesian statistics were used to moderate the standard errors within each gene and Benjamini-Hochberg's method (Benjamini and Hochberg, 1995) to adjust for multi-testing. A cut-off value of adjusted $p<0.05$ was set to assess statistical significance.

Normalized and raw data-values are deposited with GEO as series GSE10983.

7.4.10 GO-term enrichment analysis

Lists of predicted genes were examined for GO-term enrichment using R-2.5.1 (R Development Core Team, 2007) with BioConductor (Gentleman et al., 2004) and the topGO-package v. 1.2.1 using the elim algorithm to remove local dependencies between GO terms (Alexa et al., 2006). GO-term assignments were based on automatic annotation of the *A. niger* ATCC 1015 v1.0 gene models. Where nothing else is noted, $p<0.05$ is used as the cutoff for significance.

7.4.11 Synteny analysis

The finished version of the *A. niger* ATCC 1015 genome sequence was divided into fragments of 1 kb and compared to the nucleotide sequence of *A. niger* CBS 513.88 using blastn (McGinnis and Madden, 2004). A cutoff-value of 1e-75 was used. The blast results were parsed using a custom Perl script, giving for each 1 kb fragment the location of the hit, number of SNPs, insertions and deletions. The same analysis was performed for a comparison of the *A. niger* ATCC 1015 and *A. niger* ATCC 9029 genome sequences.

7.4.12 Imprint algorithm

The object of the algorithm is, for every gene sequence of *A. niger* ATCC 1015, to present the sequence from *A. niger* CBS 513.88 giving the best hit (the Imprint), so that a comparison unbiased by two sets of gene callers, can be made.

The CDSs of *A. niger* ATCC 1015 were compared to the nucleotide sequence of *A. niger* CBS 513.88 using blastn (McGinnis and Madden, 2004). The blastp output was parsed to extract for each gene the alignment to the *A. niger* CBS 513.88 sequence. This gave for each gene, the part of the CDS having a hit in the CBS 513.88 sequence, and the corresponding sequence from CBS 513.88 sequence (the Imprint). The CDS and the Imprint were compared to produce a comprehensive list of insertions, deletions, silent mutations, sense mutations, frame shift mutations and non-sense mutations for each CDS-pair. Genes with <25 % coverage in the blast hit in *A. niger* CBS 513.88 were seen as having no hit.

It was not possible to do the blastn comparison with one specific e-value cutoff, as this did not allow for alignment of short introns, while eliminating unspecific hits. Instead, the procedure described above was performed for 13 different alignments, each with a different e-value cutoff. The used e-values were 1e-5, 1e-10, 1e-15, 1e-20, 1e-25, 1e-30, 1e-35, 1e-40, 1e-45, 1e-50, 1e-75, 1e-100, and 1e-200. The 13 lists of sequences and information on the alignment were parsed to select for each gene the alignment covering the largest percentage of the putative coding sequence while still selecting the alignment with as low an e-value as possible. This gave a combined list of comparisons with one selected alignment for each gene.

This list was curated manually to remove artefacts of the blastn alignment. This was done in two ways: 1) All CDS-pairs where more than 20 nucleotides inside the alignment did not find a hit (334 pairs), were compared manually to the hit sequence to improve the alignment in hyper-variable regions. 218 alignments were improved doing this, mainly due to short exons combined with variability. The remainders were genes divided across two or more contigs in the CBS 513.88 sequence, thus making full coverage impossible. 2) All genes/Imprints pairs (629) with more than 10 SNPs/kb were pruned manually for the presence of false positive hits defined as paralogue hits. Identification of these was done by examination of the hit sequence and a list of bidirectional best hits between the two strain sequences. Although these CDSs did have blastn hits in the *A. niger* CBS 513.88 se-

quence, these have been changed to show “No hit”. Genes present both in contigs An03c0100 and An03c0110 have been pruned from the list of duplicated genes. The final summary is found at `www.computationalbiology.dk`. All genes were assigned to one of the categories of Table 7.2. Genes were only assigned to categories E–F if none of the requirements of categories G–L were fulfilled. Manual and automatic annotation was added for 9400 genes, including all genes with more than 0.5 % difference in amino acid sequence.

Acknowledgements

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Chapter 8

A systems-wide approach to understanding organic acid production in *Aspergillus niger*

> The path to my fixed purpose is laid with iron rails, whereon my soul is grooved to run. Over unsounded gorges, through the rifled hearts of mountains, under torrents' beds, unerringly I rush! Naught's an obstacle, naught's an angle to the iron way!"
> *Herman Melville — Moby Dick*

It has been subject to much discussion why *A. niger* produces organic acids in the amounts that it is capable of. If *A. niger* is grown in an unbuffered medium, it will fairly quickly acidify the medium to a pH below 2. Among several hypotheses for the purpose of this secretion, it has been suggested that the secretion of acids helps degrade the plant cell walls the saprotrophic fungus thrives on, that it slows the growth of competing organisms, and that the organic acids chelate sparse trace metals and make them available to the fungus (Pedersen et al., 2000c). Whether one or the other or a combination of these hypotheses are correct, the fact remains that *A. niger* can convert as much as 95 % of the available carbon to organic acids, making it a viable process for producing bulk chemicals (Karaffa and Kubicek, 2003).

The production of organic acids by *A. niger* has been shown in several studies to be dependent upon ambient pH. The production of oxalic acid is most efficient at pH 5–8 and is completely absent below pH 3.0 (Ruijter et al., 1999). Gluconic acid production is optimal at pH 5.5, but found at all levels of pH from 2–8 (Heinrich and Rehm, 1982, Witteveen et al., 1993). Citric acid production begins at pH 3.0 and is optimal just below pH 2.0 (Karaffa and Kubicek, 2003, Magnuson and Lasure, 2004). This suggests that an evolutionary process has selected for production of a given acid at different pH-values. In this context, the work of Ruijter et al. (1999) is interesting. They showed that a mutant strain of *A. niger*, deficient in producing gluconic acid and oxalic acid, produces citric acid at an optimum pH of 5 and without the demand for a Mn^{2+} deficient medium, which is normally essential for the production of citric acid. This suggests that the aforementioned evolution of acid production has resulted in a sophisticated system of preferred acids as a function of pH, which even ensures that another acid is produced, when conditions are unfavorable for production of the preferred acid. This leads to the hypothesis that *A. niger* strives to produce — at a given pH — the organic acid that most efficiently acidifies the medium. To test this hypothesis, the model of *A. niger* metabolism presented in chapter 3 was expanded with reactions describing the number of protons released from a given acid at a given pH based on acid disassociation constants (Figure 8.1). This allows the use of mathematical optimization principles coupled with the knowledge of metabolic pathways, and

thereby computationally determining the most efficient way of producing protons in order to acidify the surrounding medium as a function of pH. If these computations are in agreement with the pH-dependencies of the organic acids described above, it will be strong evidence that *A. niger* is evolutionally optimized for acidifying its environment.

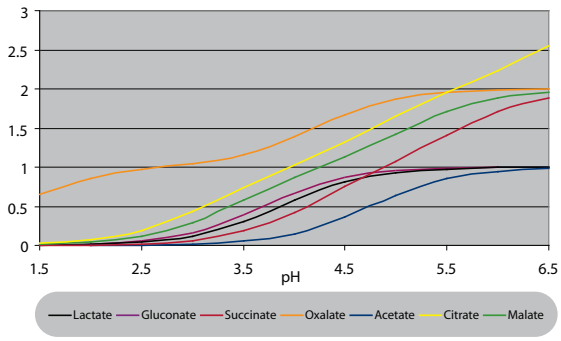

Figure 8.1: Protons per molecule of the original un-disassociated acid as a function of pH.

The response to ambient pH is not only relevant in the context of organic acid production. *A. niger* is an expression system for both homologous and heterologous proteins, and the expression of yield-lowering proteases have been shown to be dependent on pH (van den Hombergh et al., 1996). Additionally, while processes with *A. niger* have until now been considered safe for food-grade enzyme-production, a recent analysis of the *A. niger* genome (Baker, 2006) has suggested that it may be capable of producing the carcinogenic compound fumonisin B_2, which was confirmed by Frisvad et al. (2007). Also ochratoxin A has been known to be produced by *A. niger* under certain culturing conditions (Abarca et al., 1994, Samson et al., 2004). Secondary metabolite production, such as penicillin from *A. nidulans*, has in some cases been shown to be dependent on pH (Shah et al., 1991). Therefore, in addition to the model-driven investigation of the response to pH, a physiological characterization and transcriptome analysis of triplicate cultivations at pH 2.5, 4.5 and 6.0 was made to provide a systems-wide insight in the transcriptional response to ambient pH. Given that *A. niger* can grow stably at pH-values ranging from below 2 to above 8 (Hesse et al., 2002), it is reasonable to expect sophisticated transcriptional regulation. To utilize this, a methodology is presented to discover putative pH-dependent cis-acting regulatory motifs from the generated date. Using genetic engineering, this may be applied to metabolic engineering to induce the production of a given product at the pH of the process. Another analysis was on the production of organic acids as well as identification of secondary metabolite clusters responding to pH. Furthermore, the *pacC/palABCFHI* system, a conserved fungal signal transduction and transcriptional regulation system described in detail for *A. nidulans* and partially conserved in *S. cerevisiae* (Peñalva and Arst Jr, 2002, 2004), was examined and likely orthologues were found in *A. niger*.

8.1 Results

8.1.1 Modeling acid production as a function of pH

The model of chapter 3 was expanded as described in materials and methods. Acid production was simulated from pH 1.5–6.5 using two different strategies: either optimization for maximum biomass production coupled to acid generation, or optimization for maximum proton generation with a fixed biomass production. The model was allowed to use acetate, oxalate, lactate, malate, succinate, citrate, and gluconate to acidify the medium, all of acids that have been observed fermentations in our laboratory or that have been reported to be produced by *A. niger*. For each set of simulations, the acids were removed one at a time, to explore the order in which the *A. niger* simulation preferred to produce the different acids at the investigated values of pH. The complete modeling results are found in App. Figures F.1 and F.2.

Interestingly, if all acids are included, the simulations predicts oxalate as the only produced acid throughout the spectrum of pH. This is in agreement with the observation of Ruijter et al. (1999) (and the physiological characterization in the experiments shown in Figure 8.3) that oxalate is the preferred acid in a strain capable of

producing all acids.

Ruijter et al. (1999) have also reported that the production of oxalate peaks above pH 5.5, and as the calculations of Figure 8.1 show, this is the value where oxalate is fully disassociated, and the value of pH where the effect of producing oxalate for acidifying the medium levels out. The modeling results are thus in very good agreement with the hypothesis that oxalate is produced to acidify the medium, and this explains how this trait has evolved.

One could think, that since oxaloacetate hydrolase — the only enzyme producing oxalic acid in *A. niger* (Kubicek et al., 1988) — forms one mole of acetate for every mole of oxalate, acetate should also appear as a product in the model simulations. However, acetate formation is not seen, meaning that the simulations predict that it is more energetically efficient to re-metabolize this acetate that use it for acidification. This is in coherence with the report by Ruijter et al. (1999) that *A. niger* catabolizes acetate in a rate sufficient to prevent its formation during production of oxalate.

However, the modeling did not predict how oxalate production diminishes drastically below pH 3 (Ruijter et al., 1999) (Pedersen et al. (2000c) report this limit to be below pH 4), suggesting that is not due to inefficient acidification of the medium, but some other factor. To simulate this, the model was adjusted to disallow medium acidification by oxalate below pH 3 (Modeling results in Figure 8.2).

Using this model, it was found that for both modeling strategies at pH-levels 1.5–2.5, citrate is the optimal acid for medium acidification when oxalate cannot be produced. This is the same interval used for industrial production of citric acid (Karaffa and Kubicek, 2003). The necessity of the absence of oxalate production may be one reason for why very low levels of manganese are required for citrate production. Oxaloacetate hydrolase (OahA) is dependent on manganese and has a high affinity for the metal (K_m for Mn^{2+} is 4 μM (Pedersen et al., 2000c)). Deletion of *oahA* in the work of Ruijter et al. (1999) replicates this effect of manganese depletion, thereby inducing citrate production.

Further simulations removing proton-producing acids one by from the model (App. Figure F.1 and App. Figure F.2) indicates that the pH interval of 1.5–2.5 is in fact the only area where citrate is the most optimal acid (next to oxalate), indicating how the pH preference may have evolved. Another interesting finding was that gluconate is not produced in any versions of the model unless production reactions for all other acids are removed. This clearly point to that production of gluconate is not an energy-efficient method of acidifying the medium. It therefore seems likely that the efficient conversion of glucose to gluconate by *A. niger* has not evolved as a way of acidifying the medium, but to more rapidly make glucose unavailable to competing organisms. In this context, it is interesting to note that the gluconate production is more efficient around pH 5.5, a pH-level where few microorganisms have difficulty growing.

8.1.2 Physiological studies

Batch fermentations of *A. niger* BO-1 were performed in triplicates at three different pH-values (2.5, 4.5 and 6.0). For each fermentation, samples were taken for HPLC determination of sugar and acid concentrations. Profiles of the cultures are shown in Figure 8.3. Examination of Figure 8.3 shows that the biomass yield drops with increasing pH. The final biomass concentration measured decreases from 9.80 ± 0.42 g/L over 6.20 ± 1.05 g/L to 4.81 ± 0.52 g/L as pH increases (average$\pm$standard deviation). This is due to a reciprocal increase in the produced acids. Most predominantly among these is gluconate production which is not found at all at pH 2.5, but reaches as much as 10 g/L at pH 6.0. An increase in oxalate production of roughly a factor of two is also seen with each step of pH increase. Finally, pH does not seem to have an effect on the citrate production in these cultivations. This is not surprising, as manganese was added to ensure reproducible filamentous growth for the transcriptome analysis. As Dai et al. (2004) have shown, Mn^{2+} concentrations of 1000 ppb (the same as in the cultivation medium) ensures filamentous growth, however this diminishes citrate production. Citrate concentrations are low in all batches, and the citrate production is by far the

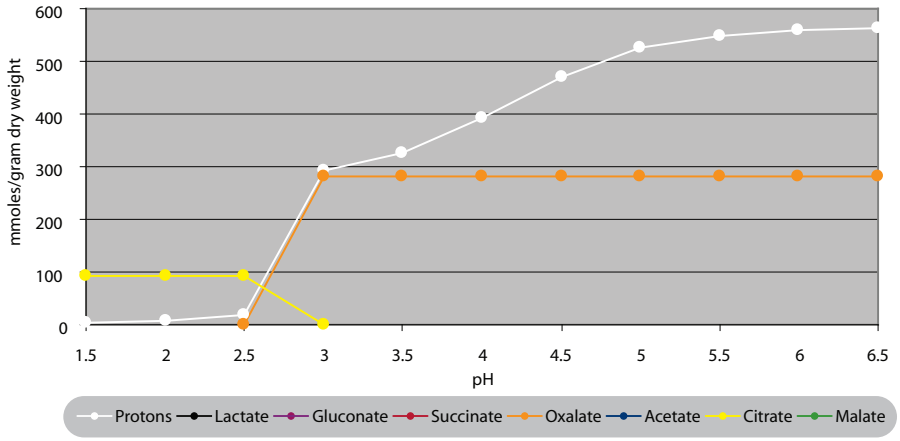

Figure 8.2: Simulated acid-production with optimization criterion of maximum protons per gram of biomass. Acid disassociation was included in the model for all of the shown species, with the exception of oxalate production below pH 3.0.

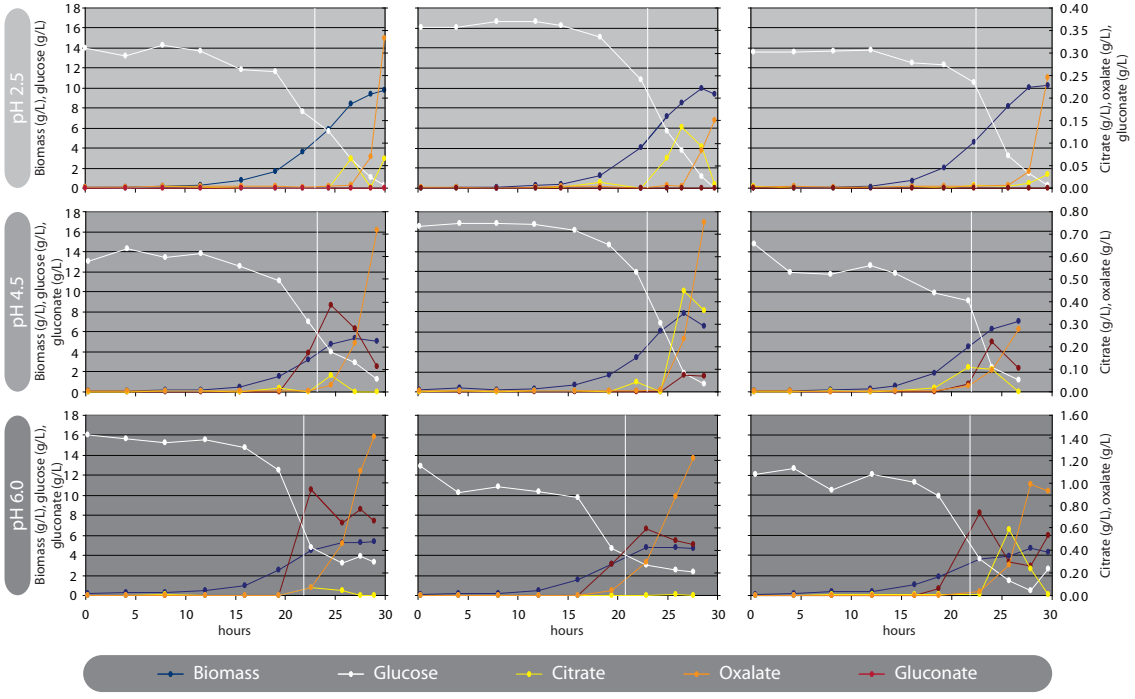

Figure 8.3: Metabolite profiles under cultivations of *A. niger* at three levels of pH. For each pH value is shown three replicates, from which biomass was sampled for transcriptome analysis. Sample times are shown with white vertical lines.

least reproducible trait across the triplicates.

From each of the nine fermentations, samples were taken for transcriptome analysis. Table 8.1 presents a summary of the growth and fermentation broth composition at the time of sampling.

As Table 8.1 shows, no significant acid produc-

Table 8.1: Biomass (dry weight), sugar, and acid concentrations for *A. niger* cultivations at three levels of pH at the time of sampling for transcriptome analysis. The calculated maximum specific growth rate is indicated. Values are shown as average±standard deviations for three replicates.

pH	Time [h]	μ_{max} [h^{-1}]	Biomass [g/L]	Glucose [g/L]	Citrate [g/L]	Oxalate [g/L]	Gluconate [g/L]
2.5	22.77±0.40	0.21±0.01	4.68±0.16	8.93±1.84	0.01±0.01	0.00±0.00	0.00± 0.00
4.5	22.72±0.63	0.21±0.01	4.40±0.47	7.87±1.97	0.05±0.05	0.02±0.02	2.39± 3.05
6.0	21.47±0.69	0.22±0.02	3.71±0.42	5.24±1.21	0.02±0.03	0.07±0.05	6.36±1.90

tion (except for gluconate production) was measured in the medium at the time of the mRNA sampling. The sampling time was chosen to be in mid-exponential phase, as the cell is in a reproducible pseudo-steady state as this time. Even though the bulk of the excretion of acid to the medium occurs in the stationary phase, this sampling time describes pH-dependent mechanisms most reproducibly. Later sampling could result in an increased effect from extracellular acids.

8.1.3 Transcription analysis

Samples were taken from the bio-reactor cultivations for transcriptome analysis. All cultures were growing as dispersed hyphal mycelium. See Table 8.1 and Figure 8.3 for details on sampling times and conditions. Data from the three biological triplicates at pH 2.5, 4.5 and 6.0 were statistically analyzed and genes that are significantly regulated (Benjamini-Hochberg corrected Bayesian p-values <0.05) in pair-wise comparisons between two pH-levels were identified. Based on the pair-wise comparisons, the regulated genes were sorted into subsets according to the direction of the statistically significant responses (Figure 8.4). Subsets will be referred to in the text by their letter.

A surprisingly large number of genes (6228) were identified to be significantly regulated in one or more of the comparisons. As the employed statistical test is a very conservative one, and more than 70 % of these genes are significant in more than one comparison, this high number should not be seen as an artefact, but rather as a combined effect of the wide range of pH and a growth effect. Especially noteworthy is the large subset J that is up-regulated at pH 2.5 and 6.0 compared to pH 4.5. It is likely that this subset is not directly regulated by pH, but rather a part of a growth effect or a stress response, as it contains a large number of housekeeping genes such as ribosomal subunits, DNA replication machinery, proteasome subunits, RNA processing machinery etc. A GO term over-representation analysis (App. F.3.3) confirmed that these terms are over-represented. The same seems to be the case for the two subsets Q and N. These subsets have the same regulatory pattern as subset J, but with one of the statistical comparisons being statistically insignificant. Therefore, clustering the genes in this manner according to the direction of the responses allows a separation of growth-related effects into subsets J, Q and N, thus leaving the remaining 2022 genes with a higher likelihood of being directly influenced by pH.

In order to examine the transcriptional regulation in the sets in more detail, a clustering algorithm was applied using transcription indices from all nine microarrays rather than averages for each group (Figure 8.4, Pane B). This method allowed more detailed differentiation between the genes and the creation of clusters within each subset. In total, 162 clusters with distinct transcription patterns across the experiments were identified. A detailed overview of the clusters is found in App. Figures F.3–F.5.

Clustering of these genes facilitates discovery of interesting co-regulations. Especially interesting for the production of gluconic acid is the observation that the cellular membrane-bound catalase (*catR*, (Fowler et al., 1993, Witteveen et al., 1992)), is tightly co-regulated with the hydrogen-peroxide and gluconic acid producing glucose oxidase (Gox/GodA; EC 1.1.3.4) (Kriechbaum et al., 1989, Frederick et al., 1990). Both are found in the same cluster of subset G in Figure 8.4. The general regulation in this subset is in good coherence with reportings that ox-

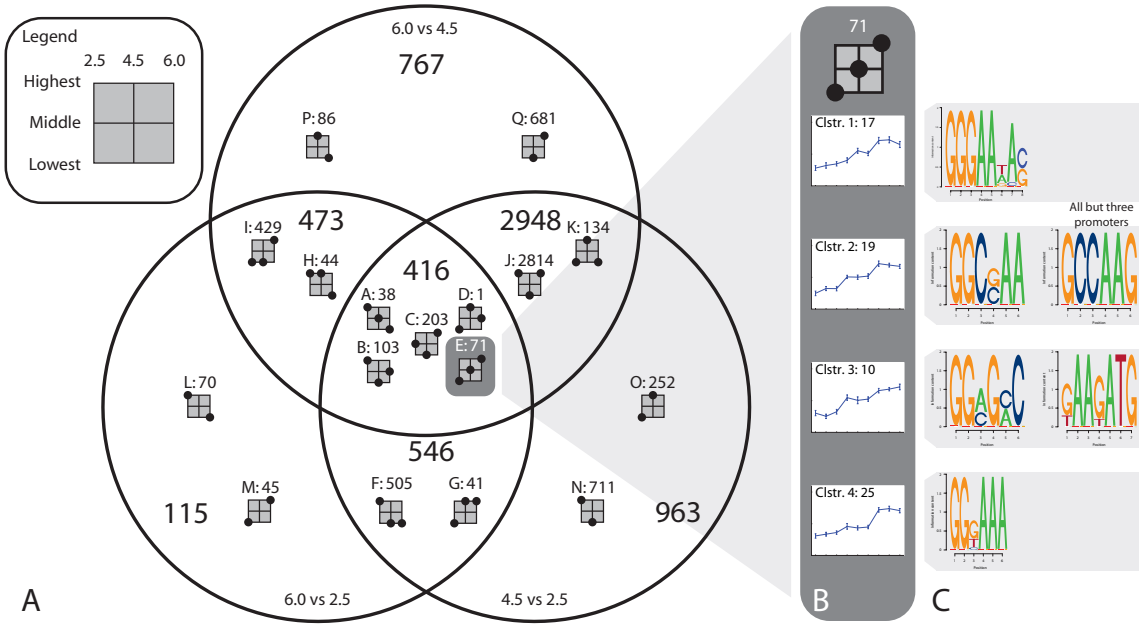

Figure 8.4: Venn diagram and clustering of significantly pH-responding genes. The Venn diagram (panel A) is based on three pairwise comparisons. Each area in the Venn diagram is divided into subsets by the direction of the response in the different comparisons. The formation of dots in the squares show the general tendency of the response, with the example of panel B having expression indices increasing with pH. Two dots on the same line means that there is no statistically significant difference between the two conditions. Each subset has been divided into clusters, as shown for the example subset (panel B). Predicted recognition-motifs for cis-acting elements are shown (panel C). Sequence logos are made as described by Schneider and Stephens (1990).

alic acid is produced in very low amounts below pH 4.5 (Heinrich and Rehm, 1982, Witteveen et al., 1993). Examination of the promoter region of the genes of that particular cluster was performed to discover potential cis-acting elements, and two motifs were found, one being 5'-GAGGWT-3' and the other 5'-ACRARAG-3'. The first motif is found nine times in the promoter of *godA*, and five times in the *catR*-promoter, making it very likely that this motif is responsible for the co-regulation of the two genes.

Another subset of special interest to acid production and regulation by ambient pH, is subset E. This subset contains three putative acid transporters, the oxalic acid producing oxaloacetate hydrolase (*oahA*) (Kubicek et al., 1988, Pedersen et al., 2000c), and the gene for a protein regulating response from neutral to alkaline pH (PacC) (MacCabe et al., 1996b). Clustering of the genes places *oahA* in cluster 1 and *pacC* in cluster 3. In light of the lack of production of acetate, it is interesting that *oahA* does not seem to be co-regulated with a potential acetyl-CoA synthase or an enzyme with a similar function. This suggesting that activation of acetate with CoA is not limiting for re-assimilation.

As an application example of the clustering, cis-acting elements have been predicted for all four clusters of the subset containing *pacC* and *oahA*. Motifs were found for each of the four clusters (Figure 8.4, panel C.), but not for the subset as a whole. A survey of subset A and the three sub-clusters (App. Figure F.3) showed that it was possible to find putative regulatory motifs for each of the sub-clusters, but not for the entire subset. That no motif could be found for the entire subset supports the strategy of dividing the subsets into clusters to find co-regulated genes.

In an examination of the predicted motifs of

subset E (Figure 8.4), the second motif for cluster 2 was found to be similar to the *A. nidulans* PacC consensus binding motif 5'-GCCARG-3' reported by Sarkar et al. (1996). This suggests that members of this group are regulated at least in part by PacC. PacC is known to be auto-regulated in *A. nidulans* (Tilburn et al., 1995, Orejas et al., 1995), and the motif is found in the *A. niger pacC* promoter as well. However, the clustering of *pacC* outside of cluster 2 suggests regulation of other factors are regulating it, giving it a slightly different transcription profile than the members of cluster 2.

Expanding the examination of the co-regulated groups of genes, information was used on the physical location of the genes on the genomic scaffolds to find 147 clusters of genes on the genome that are co-localized as well as co-regulated. Manual inspection of the clusters allowed the identification of six putative gene clusters involved in secondary metabolite biosynthesis. Two of these were found in clusters J and Q, making them less likely to be directly regulated by pH. One of the remaining four clusters is found in subset E, cluster 2 described above, and contains five co-localized and co-regulated genes. A putative gibberellin-precursor synthase (Gene ID 54123) is found in this cluster.

A specific study of the three potential citrate synthases identified by Pel et al. (2007), showed that only one is significantly regulated in any comparison, namely an up-regulation at pH 4.5 compared to pH 2.5 (An08g10920/ID 176409). This does not correspond to a pH-dependent up-regulation at pH 2.5, as would be the expected response for a citrate-synthase involved in citrate overflow metabolism. This suggests that the pH-responsive nature of citrate production is controlled at another level, i.e. transport or post-translational regulation, or that the response requires other sensing responses (manganese, high glucose etc) in addition to acidic pH.

Several industrially relevant proteins that are not discussed in detail here are found in the list of regulated genes, including the protease regulator PrtT, the acetate response regulator FacB/AcuB, α-amylases, and a large number of characterized and putative glucoside hydrolases as identified by Pel et al. (2007). A table of the 6228 regulated genes along with information on regulation and clustering is found in App. Table F.2, thus providing a catalog of information on regulation by ambient pH in *A. niger*.

8.1.4 Study of the ambient pH signal transduction pathway (*pal*) pathway

It is known that proteolytic cleavage is required for activation of PacC in both *A. nidulans* (Orejas et al., 1995, Tilburn et al., 1995, Mingot et al., 1999, Espeso et al., 2000, Díez et al., 2002) and *A. niger* (van den Hombergh et al., 1996). While the signal transduction/proteolysis pathway in *A. niger* is to our knowledge un-characterized, a two-cleavage system for inducing PacC is well described for *A. nidulans* (reviewed by Peñalva and Arst Jr (2002), Arst and Peñalva (2003) and Peñalva and Arst Jr (2004)).

The model of the pH-signaling transduction pathway in *A. nidulans* (Figure 8.5) consists of two distinct protein complexes, a plasma membrane localized sensing complex, and an endosomal membrane complex, catalyzing the first proteolytic step of PacC followed by a proteasome catalyzed cleavage to the active form.

The membrane sensing complex consists of PalF, PalH, and PalI. PalI (Arst et al., 1994, Denison et al., 1998) is a three transmembrane domain (3TMD) protein, that assists the localization of the 7TMD protein palH (Arst et al., 1994, Negrete-Urtasun et al., 1999) to the plasma membrane (Calcagno-Pizarelli et al., 2007). PalF (Caddick et al., 1986, Maccheroni Jr et al., 1997) is an arrestin-related protein that interacts directly with PalH and mediates signalling to the endosomal membrane complex through phosphorylation and ubiquitination by an unknown protein kinase and a ubiquitin ligase (Herranz et al., 2005).

PacC is a part of the endosomal membrane complex along with PalA, PalB, PalC and Vps32. PalC was first characterized by Negrete-Urtasun et al. (1999), and links the two complexes of the pH signalling pathway (Galindo et al., 2007). While it does not appear to be involved in en-

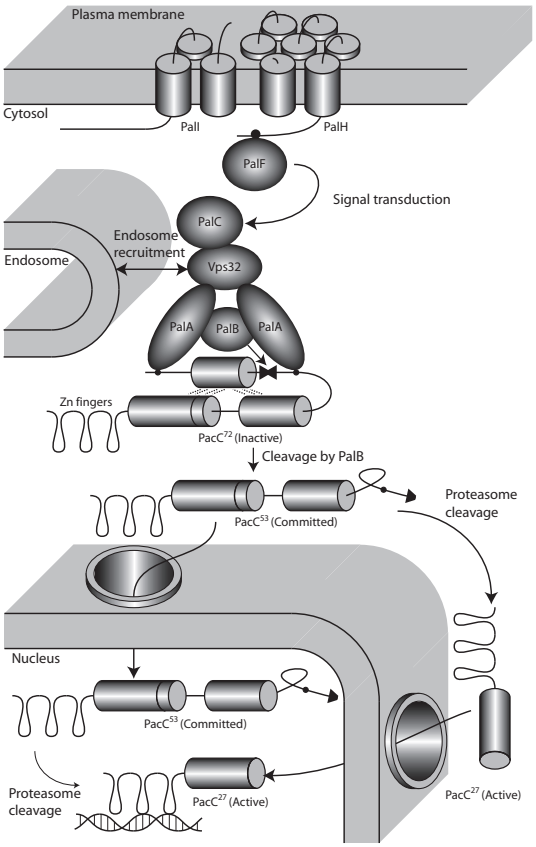

Figure 8.5: Model of pH sensing and regulation in *A. nidulans*. Black circles denote sites of protein-protein interaction, as do the overlap of two protein domains. The dotted lines of the closed conformation of PacC illustrate non-covalent interaction protecting the proteasome cleavage site. Vps32 is a part of the ESCRT-III complex that recruits to the endosome. The figure is adapted from Arst and Peñalva (2003) with information added from Tilburn et al. (2005), Herranz et al. (2005), Galindo et al. (2007), and Calcagno-Pizarelli et al. (2007).

docytosis itself, as was originally suggested by Tilburn et al. (2005), it binds Vps32/Snf7, one of four subunits of the endosomal sorting complex required for transport III (ESCRT-III) (Galindo et al., 2007). PalA binds to Vps32 and the uncleaved PacC (Vincent et al., 2003, Galindo et al., 2007) and mediates the signalling-dependent cleavage which by all evidence is performed by the calpain-like cysteine protease PalB (Denison et al., 1995, Negrete-Urtasun et al., 1997, Vincent et al., 2003, Peñas et al., 2007).

The product of the signalling dependent cleavage ($PacC^{53}$) exposes a nuclear localization signal as well as a proteasome-recognized cleavage site. The processing by the proteasome can both occur before or after localization to the nucleus, and results in the active form of PacC ($PacC^{27}$) (Hervás-Aguilar et al., 2007).

The *pal* pathway has been described as being "mechanistically dissimilar to all other known eukaryotic signal transduction pathways" (Vincent et al., 2003), and it it thus very likely that homologues of the *A. nidulans pal* genes in *A. niger* will have the same function. A survey of the genome sequence of *A. niger* found homologues of all identified genes of the signalling pathway (Table 8.2).

Table 8.2: Identified pH sensing genes in *A. nidulans* and their homologues in *A. niger*. The *A. niger* genes were identified using bi-directional best blast-hits.

Gene	**Gene models**	
	A. nidulans	***A. niger***
palA	AN4351	119792
palB	AN0256	171058
palC	AN7560	48740
palF	AN1844	Not found[a]
palH	AN6886	120044
palI	AN4853	52449
vps32/snf7	AN4240	136905
pacC	AN2855	47049

[a] No hit for palF was found in the publicly available genome sequence for *A. niger* ATCC 1015, but a near-identical hit was found on the right arm of chromosome VI in the finished version of the genome sequence.

The mRNA levels of the components of the *pal* pathway are not pH-regulated in *A. nidulans* (Negrete-Urtasun et al., 1999, Peñas et al., 2007), and a investigation of expression indices of the *A. niger* homologues indicates that these behave in the same manner. The putative *A. niger palA* and *palC* are not found to be significantly regulated in any comparison. *palB*, *palH*, *palI*, and *vps32* are significantly regulated, but are found in subsets J and Q of Figure 8.4, which is argued above to hold growth-regulated housekeeping genes. It thus seems that the *A. niger*

homologues of the *pal* pathway are independent of ambient pH as well, but may be subject to other regulation.

8.2 Discussion

Despite the great interest in organic acid production in *A. niger* — citric and gluconic acid are bulk chemicals produced by *A. niger* processes — very little work has been published on regulation by ambient pH in *A. niger*. This study examines the response to ambient pH using two distinct strategies. One is a strictly hypothesis-driven application of stoichiometric modeling, where the modeling results are compared to reported observations with the objective to see in which cases the hypothesis of *A. niger* being optimized through evolution for acidification at any given pH, holds. The other, the transcriptomic, study is a more classical application of systems biology, in that it is a data-driven study, and the results allow the generation of new hypotheses and present a data-set useful for *A. niger* and pH-regulation researchers in general. The types of conclusions that can be deduced from the two parts of this study are thus fairly different in nature, and for this reason they will be discussed separately.

The modeling part of the study has shown that the optimum pH-intervals for production of acids, and the types of acids produced at certain pH-values, can to a certain extent be explained and simulated for citrate and oxalate, based on an assumption of an evolutionary selection for efficient acidification. The success of this approach to modeling acid production strongly suggests that *A. niger* has not evolved to outgrow its competitors as *E. coli* or have a very efficient glucose uptake like *S. cerevisiae*. Instead, *A. niger* metabolism seems to be optimized to produce the most protons from the sparse nutrients available in a saprophytic environment. This also implies that acid production in *A. niger* does not stem from over-flow metabolism, but rather from a survival objective of proton production, at least for oxalic acid and citric acid.

The inability of the model to predict the pH-optimum of gluconic acid production suggests that the main objective of gluconic acid production is not related to acidification of the medium. This is supported by the detailed on-line fermentation chromatography results presented by van de Merbel et al. (1994), where glucose in the medium is rapidly converted fully into gluconic acid, which thereafter functions as a substrate for the rest of the fermentation. As the modeling only can compute conditions after a full degradation of the substrates, this will not show in the model. The production of gluconic acid thereby seems to be a method of making glucose unavailable to other competing organisms. It also fits with the observations of Figure 8.3, where gluconic acid, that was produced early in the fermentation, is seen to be re-consumed later.

While the cellular response to manganese deficiency is undoubtedly complex, as the work of Dai et al. (2004) and others have shown, it is interesting that the results of Ruijter et al. (1999) indicate that the citrate production becomes insensitive to manganese concentrations by the deletion of glucose oxidase and oxaloacetate hydrolase. While the applied model does not include the effects of manganese deficiency, it was able to replicate the effect of citrate being produced in an oxalate-deficient strain. While the absence of manganese presumably has other effects improving citrate yields, it seems based on these results that the main reason for its effect is that oxaloacetate hydrolase is dependent on manganese.

As the results of the modeling studies using growth-optimization state (App. Figure F.1), the ratio between acid and biomass production as a function of the pH is inverse in the modelled results and the experimental results. One reason for this effect is that it is very unlikely that the acid regulation systems of *A. niger* were evolved in a medium as heavily buffered as a controlled bio-reactor with pH regulation. It is thus efficient at a high pH to sacrifice biomass production for the production of large amounts of protons to quickly lower the pH, and reduce this production at low pH-values. We have not attempted to model this behavior as there is very little available detailed data on acid production at different pH-values. The work by Pedersen et al. (2000b) is of sufficient detail, and thus this

was used to approximate a constant ratio of protons to biomass. While the assumption of a constant proton/biomass ratio is not valid over the full range of pH, it does allow us to study the simulated response in detail across the range of pH shown. Changing the proton/biomass ratio for individual pH-values would only change the magnitude of the acid production, and not the species.

In examining the transcriptional response, it was interesting — in the context of organic acids — to see that *oahA* is expressed and regulated while there is no significant acid production at the time of sampling for transcriptome analysis (Table 8.1). This suggests retention of the acid inside the cells or regulation of the gene-product at a post-translational level.

In total, the number of genes influenced by ambient pH was surprisingly high. While the transcriptional analysis is to some extent confounded by a effect on "domestic" genes, the remaining response still high. This response is not unlikely as *A. niger* growing in nature acidifies the surroundings, thus living through a scale of pH-values. This presumably requires a flexible and dynamic response. Another point is, as Arst Jr and Peñalva (2003) correctly argue, that when transcription of a gene is affected by ambient pH, does not necessarily mean that it is regulated by pH. It may be an indirect consequence caused by differences in uptake efficiencies, intracellular metabolite levels, or other indirect effects. This might well be the case here.

The applied two-step clustering methodology allows us the differentiation between different effects, although it cannot determine which clusters of genes are directly or indirectly influenced by pH. One interesting application of this transcription study and the clustering is the prediction of regulatory motifs based on the transcription profiles. While this in theory could be done for all of the 162 identified clusters, the performed predictions are limited to the ones described in the main matter of this study, but details on the clusters are provided in Apps. F.3–F.5 and App. Table F.2. This is due to the relative large amount of analysis time it takes to identify each motif, but the provided catalog of transcription will allow for proposition of further hypotheses by other researchers.

The analysis of the clusters also includes the physical location of the genes. For the clusters predicted to be involved in secondary metabolite production, this physical location adds considerable value to the transcriptome analysis. It is confirmed that putative secondary metabolite clusters is transcriptionally regulated by pH. Even so, some of the identified co-regulated gene clusters may be artefacts, due to errors in gene calling. E.g. if a gene erroneously has been predicted to be several genes, these will be seen as being co-regulated in the transcriptome analysis. Another likely explanation is that they are co-regulated by a common promoter region. However, for clusters of more than two genes, this is unlikely to to be the case.

The first steps towards understanding the pH signalling pathway of *A. niger*, a pathway of great potential importance for the fermentation industry, are provided. The investigation of the *A. niger* homologue to the — in *A. nidulans* — well-described *pal* pH signalling pathway, showed that all components are present in *A. niger*, and expressed independently of pH. The uniqueness of this pathway makes it more than likely that these genes code for orthologues of the *A. nidulans* genes. However, a classical phenotypical characterization of mutants is still necessary to finally establish the function, but with this study, the targets for this characterization are now firmly established.

8.3 Materials and methods

8.3.1 Modeling acid production

For each pH-value a set of reactions were added to the model of chapter 3, thereby creating a new model for each level of pH. The reactions set consisted of seven reactions, one for each of the acids included in the model. Each reaction contains the fully protonated acid in an equilibrium with the partially unprotonated acid species and a number of protons. This number was calculated for each pH and acid using the acid dissociation constant equation as shown in equation 8.2.

$$K_a = \frac{[H^+][A^-]}{[HA]} = 10^{-pH}\frac{[A^-]}{[HA]} \Rightarrow \quad (8.1)$$

$$\frac{[A^-]}{[HA]} = \frac{K_a}{10^{-pH}} \quad (8.2)$$

In the case of poly-protic acids such as citric acid, a set of coupled equations — one for each acid group — was used. An example for citrate at pH 4.5 is shown in equation 8.3 (Full set described in App. Table F.1).

$$\text{CITe} < - > \text{CIT-e} + 1.3196\ \text{H+e} \quad (8.3)$$

The entity CIT-e of equation 8.3 is a mixed species, composed of citric acid molecules in various degrees of de-protonation, all in equilibrium at the given pH. It is assumed that the acids are transported across the cytoplasmic membrane fully protonated.

Modeling of acid production was performed using stoichiometric matrices and linear programming for solving them, as described in Andersen et al. (2008a). Either the solving objective was a maximization of proton-production with a fixed biomass production of one gram or maximization for growth (growth-coupled proton-production). For modeling of growth-coupled proton-production, the biomass equation was added a demand for 15.3 mmoles of protons pr. gram of dry-weight. This value was calculated from the oxalate and citrate yields of a pH 6.0 cultivation described by Pedersen et al. (2000b). All simulations were performed with 100 mmoles of glucose and unlimited ammonium as substrates.

8.3.2 Fermentation procedure

Strains

The strain used was *A. niger* BO-1, obtained from Novozymes A/S and maintained as frozen spore suspensions at -80°C in 20 % glycerol.

Growth media

Complex medium: 2 g/L yeast extract, 3 g/L tryptone, 10 g/L glucose monohydrate, 20 g/L agar, 0.52 g/L KCl, 0.52 g/L $MgSO_4 \cdot 7H_2O$, 1.52 g/L KH_2PO_4 and 1 mL/L of trace elements solution. Trace element solution: 0.4 g/L $CuSO_4 \cdot 5H_2O$, 0.04 g/L $Na_2B_4O_7 \cdot 10H_2O$, 0.8 g/L $FeSO_4 \cdot 7H_2O$, 0.8 g/L $MnSO_4 \cdot H_2O$, 0.8 g/L $Na_2MoO_4 \cdot 2H_2O$, 8 g/L $ZnSO_4 \cdot 7H_2O$. Batch cultivation medium: 20 g/L glucose monohydrate, 2.5 g/L $(NH_4)_2SO_4$, 0.75 g/L KH_2PO_4, 1.0 g/L $MgSO_4 \cdot 7H_2O$, 1 g/L NaCl, 0.1 g/L $CaCl_2 \cdot 2H_2O$, 0.05 mL/L antifoam 204 (Sigma) and 1 mL/L trace element solution. Trace element solution composition: 7.2 g/L $ZnSO_4 \cdot 7H_2O$, 0.3 g/L $NiCl_2 \cdot 6H_2O$, 6.9 g/L $FeSO_4 \cdot 7H_2O$, 3.5 g/L $MnCl_2 \cdot 4H_2O$ and 1.3 g/L $CuSO_4 \cdot 5H_2O$.

Preparation of inoculum

Fermentations were initiated by spore inoculation to a final concentration of 2×10^9 spores/L. Spores were propagated on complex media plates and incubated for 7–8 days at 30°C before being harvested with 10 mL of 0.01 % Tween 80.

Batch cultivations

Batch cultivations were performed in 2 L Braun fermenters with a working volume of 1.6 L, equipped with three Rushton four-blade disc turbines. The bio-reactor was sparged with air and the concentrations of oxygen and carbon dioxide in the exhaust gas were measured in a gas analyzer. The temperature was maintained at 30°C. The pH was controlled by automatic addition of 2 M NaOH. Agitation and aeration were controlled throughout the cultivations. For inoculation of the bioreactor, the pH was adjusted to 2.5, stirring rate 100 rpm and aeration 0.1 vvm. After germination, the stirring rate was increased to 300 rpm and the air flow to 0.5 vvm. 11–12 hours after inoculation, the stirring rate was increased to 600 rpm and the air flow to 1 vvm. When the CO_2 in the exhaust gas reached a value of 0.1 %, the stirring rate was set to 1000 rpm and the pH was slowly increased to 4.5 or 6.0 with a drop of 2 M NaOH every 10 seconds if needed.

The concentrations of oxygen and carbon dioxide in the exhaust gas were monitored with a gas analyzer (1311 Fast response Triple gas, Innova combined with multiplexer controller for Gas Analysis MUX100, B. Braun Biotech International).

Sampling

Cell dry weight was determined using nitrocellulose filters (pore size 0.45 μm, Gelman Sciences). The filters were pre-dried in a microwave oven at 150 W for 15 minutes, cooled in a desiccator and subsequently weighed. A known volume of cell culture was filtered and the residue was washed with 0.9 % NaCl and dried on the filter for 15 minutes in a microwave oven at 150 W and cooled in a desiccator. The filtrate was saved for quantification of sugars and extracellular metabolites and stored at -80°C. The filter was weighed again and the cell mass concentration was calculated. These values were used to calculate maximum specific growth rates. For gene expression analysis, mycelium was harvested at the mid-late exponential phase (at approximately half the maximum concentration of biomass) by filtration through sterile Mira-Cloth (Calbiochem) and washed with a PBS buffer (8 g/L NaCl, 0.20 g/L KCl, 1.44 g/L Na_2HPO_4 and 0.24 g/L KH_2PO_4 in distilled water). The mycelium was quickly dried by squeezing, and subsequently frozen in liquid nitrogen. Samples were stored at -80°C until RNA extraction.

Quantification of sugars and extracellular metabolites

The concentrations of sugar in the filtrates were determined using HPLC on an Aminex HPX-87H ion-exclusion column (BioRad, Hercules, CA). The column was eluted at 60°C with 5 mM H_2SO_4 at a flow rate of 0.6 mL/min. Metabolites were detected with a refractive index detector and a UV detector.

8.3.3 Transcriptome analysis

Extraction of total RNA

40–50 mg of frozen mycelium was placed in a 2 mL Eppendorf tube, pre-cooled in liquid nitrogen, containing three steel balls (two balls with a diameter of 2 mm and one ball with a diameter of 5 mm). The tubes were then shaken in a Mixer Mill, at 5°C for 10 minutes, until the mycelium was ground to powder. Total RNA was isolated from the powder using the Qiagen RNeasy Mini Kit, according to the protocol for isolation of total RNA from plant and fungi. The quality of the extracted total RNA was assessed using a BioAnalyzer 2100 (Agilent Technologies Inc., Santa Clara, CA, USA) and the quantity determined using a spectrophotometer (GE Healthcare Bio-Sciences AB, Uppsala, Sweden). The total RNA was stored at -80°C until further processing.

Preparation of biotin-labeled cRNA and microarray processing

15 μg of fragmented biotin-labeled cRNA was prepared from 5 μg of total RNA and hybridized to the 3AspergDTU GeneChip (Andersen et al., 2008b) according to the Affymetrix GeneChip Expression Analysis Technical Manual (Aff, 2007).

cRNA was quantified in a spectrophotometer (same as above). cRNA quality was assessed using a BioAnalyzer. A GeneChip Fluidics Station FS-400 (fluidics protocol FS450_001) and a GeneChip Scanner 3000 were used for hybridization and scanning.

The scanned probe array images (.DAT files) were converted into .CEL files using the GeneChip Operating Software (Affymetrix).

Analysis of transcription data

Affymetrix CEL-data files were preprocessed using the statistical language and environment R (R Development Core Team, 2007) version 2.5.1. The probe intensities were normalized for background using the RMA method (Irizarry et al., 2003) using only perfect match (PM) probes. Normalization was performed subsequently using the quantiles algorithm (Bolstad et al., 2003). Gene expression values were calculated from the PM probes with the medianpolish summary method (Irizarry et al., 2003). All statistical preprocessing methods were used by invoking them through the affy package (Gautier et al., 2004).

Statistical analysis was applied to determine genes subject to differential transcriptional regulation. The limma package (Smyth, 2004) was used to perform moderated t-tests between two sets of triplicates from each pH level. Empirical Bayesian statistics were used to moderate the

standard errors within each gene and Benjamini-Hochberg's method (Benjamini and Hochberg, 1995) to adjust for multi-testing. A cut-off value of adjusted p<0.05 was set to assess statistical significance.

Normalized and raw data-values are deposited with GEO as series GSE11725.

8.3.4 Clustering

The 6228 genes that were significantly regulated in one or more pairwise comparisons were sorted into groups based on their regulation in the three different sets of conditions. These groups were divided into a varying number of subgroups (clusters) using the clustering algorithm ClustreLustre (Grotkjaer et al., 2006), using k-means normalization. The groups were divided until all clusters had a minimum separation distance of 1.01. This number was picked empirically and was the minimum distance where each cluster still had a distinct regulation pattern.

8.3.5 Identification of co-regulated gene clusters

Co-regulated gene-clusters were defined in this study as genes on the same scaffold that are separated by no more than 5 kilobases, significantly regulated in one or more pair-wise comparison, and having the same regulation pattern as determined by the detailed clustering using ClusterLustre.

8.3.6 Prediction of conserved motifs

Conserved motifs were predicted using R 2.6.2 (R Development Core Team, 2007) with the cosmo package v. 1.4.0 (Bembom et al., 2007). Default settings were used with the following exceptions: A background Markov model was computed using the intergenic regions from scaffold 1 of the *A. niger* ATCC 1015 genome sequence. Intergenic regions containing unknown bases (N's) were pruned from the training set amounting to 1.7 Mb in 1214 sequences. The Two-Component-Mixture (TCM), One Occurrence Per Sequence (OOPS) and Zero Or One Occurrence Per Sequence (ZOOPS) motif models was used to search for conserved motifs. For all query-sequences was used 1000 base pairs up-stream of the start codon of the gene or of the predicted transcription start, if one such was found. If a transcription start was predicted, the sequence from this base pair and to the start codon was included as well, thus increasing the length of sequence to more than 1 kilobase.

8.3.7 GO-term enrichment analysis

Significantly regulated subsets of genes were examined for GO-term enrichment using R-2.5.1 R Development Core Team (2007) with BioConductor Gentleman et al. (2004) and the topGO-package v. 1.2.1 using the elim algorithm to remove local dependencies between GO terms Alexa et al. (2006). GO-term assignments were based on automatic annotation of the *A. niger* ATCC 1015 v1.0 gene models. Where nothing else is noted, p<0.05 is used as the cutoff for significance.

Acknowledgements

Linda Lehmann is acknowledged for performing the cultivations and some of the microarray hybridizations. Antonio Diego Martinez for kindly supplying the genome coordinates for the predicted genes of *A. niger* ATCC 1015. Lene Christiansen for indispensable practical assistance with array preparations. Tina Johansen for excellent technical support on fermentation equipment. Martin Nielsen for assisting with the design of an stable and dynamic pH controlling algorithm. Scott E. Baker for allowing the use of the finished version of the genome sequence of *A. niger* ATCC 1015.

Chapter 9

Network-based analysis of carbohydrate-active gene transcription in *Aspergillus niger*

> "Quotation is a serviceable substitute for wit"
> *Oscar Wilde*

Expression profiling of extracellular enzymes is of high relevance to several industries. Commercial enzyme-preparation are often targeted to a specific activity such as cellulase for the degradation of cellulose and preparation of fabrics or amylases for the preparation of dense syrups from starch or similar compounds. The world market for industrial enzymes is thus, as discussed in section 2.2, a multi-billion dollar market. Another emerging market of great potential is the production of second generation bio-fuel. Energy-efficient processes are relying on enzymes produced by fungi and other degraders of dead biomass to produce cheap CO_2-neutral ethanol from non-edible plant matter (Galbe and Zacchi, 2007). The enzymes of *A. niger*, it being a saprotrophic fungus, are of interest to this process.

The interest in profiling the expression patterns of these enzymes is not new, but few large-scale surveys have been done. An early study was made by de Vries et al. (2002) using Northern blotting to create expression profiles of 26 pectinolytic genes under 16 different growth conditions. The publication of the first *A. niger* genome by Pel et al. (2007) provided the prediction of 171 polysaccharide-active enzymes, along with microarrays for expression profiling. This has catalyzed more research, specifically the work of Martens-Uzunova et al. (2006), where expression profiles of 21 pectinolytic genes are examined, the work of Yuan et al. (2006, 2008a), where the genes for the degradation of the polysaccharide inulin are examined, and the regulating protein identified, and the latest work of Yuan et al. (2008b); expression profiling of genes from glucoside hydrolase families 13, 15, and 31.

However, while enzyme preparations are often sold to target a specific class of compounds, the polysaccharides are rarely found independently in nature. Hemicelluloses, found in the cell walls of plants, are a complex and tangled web of several types and structures of poly-saccharides such as glucomannan, arabinan and xylan. It has been shown in several studies (vd Veen et al., 1993, Flipphi et al., 1994, de Vries et al., 2002a), that the presence of one simple saccharide can trigger the expression of enzymes for the degradation of an entirely different structure (as was shown to be the case with xylose in chapter 6). Another possibility, that has industrial applications, is the use of a cheap carbon-source to induce the enzymes required for degradation of a more complex and expensive one Ruttkowski

et al. (1991), de Vries et al. (2002a). One example is the work of Yuan et al. (2006), where sucrose induces the genes for all of the enzymes required for degrading inulin.

With the complex regulation of expression of a large number of different enzymes and the fact that many different enzymes are needed for the utilization of certain carbon sources, it is necessary to apply a systems-wide approach for mapping the regulatory network. The enzyme expression network can be combined and cross-triggered, so being able to examine the entire system at once can shed light on systems that might not be possible to pre-empt with a hypothesis-driven approach.

In this study, knowledge on the structure and degradation of 16 types of plant polysaccharides was compiled from literature and combined with information on the putative genes coding for carbohydrate-active enzymes from Pel et al. (2007) as well as characterized genes from sequence databases. This has been systematized in a graphical representation of the polysaccharide structures, allowing an overview of 188 genes coding for carbohydrate-active enzymes and enzymatic activities predicted to degrade specific bonds in the polysaccharide structures. A feature of this mapping allows the plotting of gene-related data, such as transcription data, onto the map. This makes it possible to highlight directly on the polysaccharide structures e.g. which genes are actively induced on a specific carbon source. This is in fact a network-based approach for interpretation of the data, where the network is provided by the structures of the extracellular polysaccharides, in contrast to the intracellular metabolic or regulatory networks often used for data-interpretation.

To demonstrate how enzyme interaction graphics can be used to visualize the global transcription response and allow the detection of cross-induction, transcriptomics was performed on batch cultivations on three monosaccharides and three complex carbohydrates with defined compositions. The DNA microarray described in chapter 6 was used for all analyses.

9.1 Results and discussion

9.1.1 Polysaccharide mapping

In a review of the available literature on the degradation of polysaccharides by *A. niger*, information was compiled on the following 10 types of polysaccharides: starch, cellulose, pullulan, inulin, galactomannan, galactoglucomannan (soluble and insoluble), xyloglucan (types XXGG and XXXG), as well as the following six distinct components of pectin: smooth pectin (pectate), xylogalacturonan, arabinogalactan (type I and II, also known as protein-bound arabinogalactan), arabinan and rhamnogalacturonan I. The last known polysaccharide component of pectin, rhamnogalacturonan II, was not included even though the structure has been elucidated (Pérez et al., 2003), since no studies of its degradation by *A. niger* was found in the literature search. Analyses of the degradation of this polysaccharide would be made additionally difficult by the fact that it is composed mainly of highly modified and rare sugars and thought to be the most complex polysaccharide on Earth (Pérez et al., 2003).

The information on the structures have been gathered in schematic representations of each of the polysaccharide type. An example of this (for soluble galactoglucomannan) is found in Figure 9.1. Schematic representations for the remaining 15 structures and information on the genes are found in App. Figure G.1–G.15.

For each of these structures, the available literature and sequence databases (Swissprot/Uniprot `http://www.expasy.org/sprot/`) were examined and information was gathered on the enzymes required for their degradation. This was integrated on the schematic representation of the structure as EC numbers where available, or as enzyme-names if the EC number was not available (As demonstrated in Figure 9.1). This was compared to the annotation of *A. niger* CBS 513.88 genome sequence (Pel et al., 2007) to identify putative isoenzymes for each activity. For each structure, this has resulted in a table containing the activities required for degradation, reference to literature on the characterization of the genes and enzymes, as well as information on the specificities where available. The

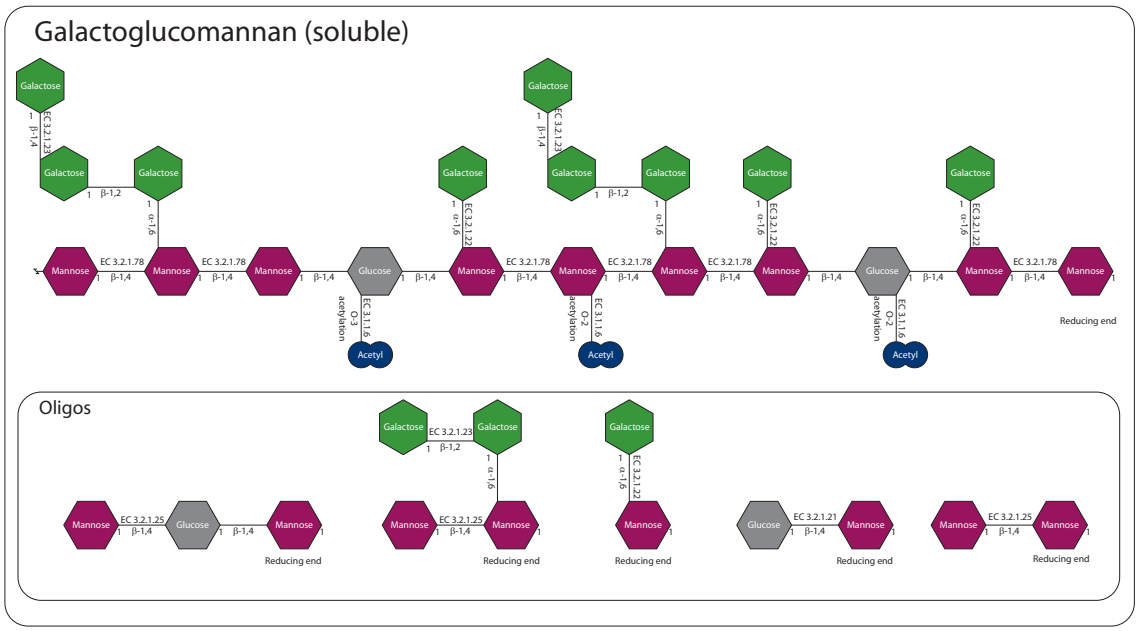

Figure 9.1: Schematic representation of soluble galactoglucomannan. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on the reportings of Sims et al. (1997), Schröder et al. (2001), de Vries and Visser (2001), and Capek et al. (2002).

sequence information is found as Uniprot accession numbers as well as gene IDs in the *A. niger* CBS 513.88 and ATCC 1015 sequence. An example of this is found in Table 9.1, with the full table and tables for all 16 structures found in App. Tables G.1–G.16. This annotation is a valuable reference on carbohydrate degradation by *A. niger*.

For a number of the studies found in the literature search, it was not possible to link the characterized enzymes with a sequence as only molecular mass and/or isoelectric point of the characterized enzyme(s) were given. These values differ from those predicted from the sequence information as the extracellular enzymes are often glycosylated proteins, which affects the determination of the molecular mass and changes the isoelectric point. Furthermore, many of the proteins are cleaved one or more times in the signalling and secretion process. However, as these characterizations still include valuable information on the enzymatic capabilities of *A. niger*, App. Table G.17 includes an overview literature on characterizations of 24 enzymatic activities, where the gene could not be determined.

The mapping of these 16 structures includes information on 115 unique putative and characterized carbohydrate active genes from the *A. niger* CBS 513.88 sequence, and 106 from the *A. niger* ATCC 1015 sequence (117 unique genes). Of these, the products of 57 of the genes have been previously characterized (See App. Tables G.1–G.16 for references). In total, the integrated information includes references to 205 articles. A full overview of the structures and the integrated genes (based on the genome sequence of *A. niger* ATCC 1015 as presented in chapter 7) can be downloaded from `www.computationalbiology.dk/`. This map also

Table 9.1: Extract of the table of the enzymatic activities required for the degradation of soluble galactoglucomannan by *A. niger* (App. Table G.6). For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes are gathered from the work of Sims et al. (1997), Schröder et al. (2001), de Vries and Visser (2001), and Capek et al. (2002).

EC number	Name	Gene characterization	Specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.78	Endo-1,4-β-D-mannanase	Ademark et al. (1998)	Ademark et al. (1998)			An05g01320	50378
3.2.1.78	Endo-1,4-β-D-mannanase					An15g07760	40875
3.2.1.25	β-mannosidase					An01g06630	172587
3.2.1.25	β-mannosidase	Ademark et al. (1999, 2001a), Bouquelet et al. (1978)	Ademark et al. (1999, 2001a)	**mndA**	Q9UUZ3	An11g06540	138876
3.2.1.22	α-galactosidase	Ademark et al. (2001a), de Vries et al. (1999a)	Ademark et al. (2001a)	**aglC**	Q9UUZ4	An09g00260	212736
3.2.1.22	α-galactosidase					An01g01320	172232
3.2.1.22	α-galactosidase	de Vries et al. (1999a), Manzanares et al. (1998)		**aglB**	Q9Y865	An02g11150	207264
3.2.1.22	α-galactosidase	den Herder et al. (1992), de Vries et al. (1999a), Wallis et al. (2001)		**aglA**	A2QL72	An06g00170	37736
3.2.1.21	β-glucosidase					An15g04800	181816
3.2.1.21	β-glucosidase					An17g00520	129891
3.2.1.21	β-glucosidase	Witte and Wartenberg (1989), Dan et al. (2000), Ramirez-Coronel et al. (2003), Seidle et al. (2004), Seidle and Huber (2005), Seidle et al. (2005, 2006)		**bgl1**	A2RAL4	An18g03570	56782
3.2.1.23	β-galactosidase					An01g10350	46429
3.2.1.23	β-galactosidase					An14g05820	41910
3.2.1.23	β-galactosidase	de Vries et al. (1999a)		**lacA**	P29853	An01g12150	51764
3.1.1.6	Acetyl esterase					An02g02540	N/A

includes a section with an overview of all of the 171 genes identified to code for putative or known polysaccharide-acting enzymes sorted into gene families.

This map has been implemented in the ReMapper software (Chapter 4), which allows for plotting of expression indices directly on the structures as well as in the overview section, thus making a systems-wide examination possible. This tool was applied in the following study of gene expression on different carbon sources.

9.1.2 Transcriptome analysis

To assess the regulatory network of genes for extracellular enzymes, *A. niger* was cultivated on six different carbon sources: three monosaccharides (glucose, arabinose and xylose), and three complex polysaccharides with a defined composition of sugars (starch, arabinan and oat spelt xylan). Crude preparations of polysaccharides may include a multitude of undefined sugars and other types of compounds. The use of defined complex polysaccharides in this type of analysis allows for stronger conclusions on which saccharides induce which genes.

The batch cultivations were performed in shake flasks and samples were taken for transcriptome analysis and determination of free sugar concentrations (Table 9.2). Pairwise statistical comparisons of data from the sets of biological replicates were performed, and the number of statistically significantly (Benjamini-Hochberg adjusted p-values < 0.05) regulated genes in each comparison is shown in Table 9.3.

In an examination of the sugar-concentration measurements of Table 9.2, it is rather clear, that the sugar-profiles at the time of sampling for transcriptome analysis are quite different. The only exception is the profiles on the glucose and starch media, where the concentrations of free glucose are rather similar. This is most likely due to the fact that the strain employed is an amylase-producer, meaning that starch is rapidly be hydrolyzed to glucose, thus making

Table 9.2: Biomass and sugar concentrations at the time of RNA-sampling from cultivations on six different carbon sources. All values are shown as average±standard deviation. Cells marked with - were not measured.

Carbon source	Biomass [g/L]	Xylose [g/L]	Arabinose [g/L]	Glucose [g/L]
Arabinan	4.28±0.42	0.00±0.00	0.87±0.35	-
Arabinose	5.72±0.30	0.00±0.00	6.76±1.02	0.00±0.00
Glucose	6.49±0.96	-	-	6.26±0.84
Starch	7.49±0.60	-	-	4.23±0.10
Xylan	9.00±0.36	0.66±0.09	0.12±0.11	-
Xylose	6.24±0.21	6.39±2.92	-	-

the actual difference between the two carbon sources small. This is reflected in the transcriptome comparison of Table 9.3, where it is seen that only 27 genes are significantly regulated between glucose and starch. These genes are most likely responding to poly-saccharides present in the degraded starch medium.

Further examining Table 9.3, it is seen that a larger number of genes are responding to the polysaccharides xylan and arabinan compared to the monosaccharides and starch. This is expected since degradation of the diverse components and types of covalent bonds constituting complex carbon sources must require a larger set of genes than a simple one-sugar monosaccharide substrate. Furthermore, as can be seen in Table 9.2, the concentration of free sugars is roughly an order of magnitude lower in the medium containing the complex carbon sources. de Vries et al. (1999b) showed that CreA-mediated carbon repression of xylanolytic enzymes by xylose begins at 0.15 g/L and increases in strength up to in the area between 4.5–10.5 g/L, which is similar to the concentrations in the comparison of xylose and xylan in this study. The free sugars are seemingly released from the polysaccharides (except starch) in a rate that effectively lessens the effects of carbon repression on these media.

The differences in induction were examined using the mapping technique described in section 9.1.1, and for each pairwise comparison a map was made to explore the statistically significant regulations. A few example comparisons that showed results on a systemic level are discussed here:

Arabinan versus arabinose: The comparison of these two carbon sources (App. Figure G.16) showed a diverse response. Regulation was found in 27 of the 36 carbohydrate-acting gene families predicted to be present in *A. niger* (Pel et al., 2007). As the mapping shows, the induction on arabinan includes unsurprisingly all of the activities required to degrade arabinan (as described in App. Table G.15), but also the entire sets of genes required to degrade the pectin components xylogalacturonan, arabinogalactan and rhamnogalacturonan. This is very likely due to the presence of small amounts of rhamnose, galactose, and galacturonic acid in the preparation of arabinan, as described in the materials section. Galacturonic acid is known to induce pectinolytic enzymes (Ruttkowski et al., 1991, de Vries et al., 2002a). The induction on arabinan also includes activities directed towards acid-residues not described in the arabinan preparation, such as genes putatively acting on glucuronic acid of arabinogalactan as well as rhamnogalacturonan acetyl esterase (*rgaeA*), and ferulic acid esterase B (*faeB*) acting on arabinan. These enzymes are reacting to compounds found in arabinan and rhamnogalacturonan I (where arabinan is a component, see App. Figures G.14 and G.15). It is therefore equally likely that triggering residues are present in minute amounts in the preparation or these genes are induced by arabinan.

Starch versus glucose: This comparison had 27 differentially regulated genes, and only one of them is coding for a carbohydrate-acting enzyme (App. Figure G.17). This one gene is the endo-glucanase *xeg12A*, shown to be specific

Table 9.3: Overview of significantly regulated genes between cultivations on six different carbon sources. The first number in the cells is the number of significantly regulated genes in the pairwise comparison of the carbon sources in the top row and left column. The number marked with an ↑ are the genes that are up-regulated on the carbon source in the top row relative to the one in the left column, while the number with an ↓ denotes the opposite.

	Xylan	**Starch**	**Arabinan**	**Xylose**	**Glucose**
Arabinose	991 (318↑/673↓)	220 (110↑/110↓)	1281(1048↑/233↓)	25 (6↑/19↓)	92 (16↑/76↓)
Glucose	1087 (375↑/712↓)	27 (17↑/10↓)	1874 (1485↑/389↓)	59 (50↑/9↓)	
Xylose	387 (109↑/278↓)	124 (52↑/72↓)	1844 (1449↑/395↓)		
Arabinan	2999 (509↑/2492↓)	1936 (473↑/1463↓)			
Starch	361 (127↑/234↓)				

for the β-1,4-glycosyl-bonds of un-branched glucose units in the xyloglucan backbone (Master et al., 2008). It thus seems to serve as a "scouting" enzyme that is induced by poly-glucosides produced in the degradation of starch, even though no β-1,4-glycosyl-bonds are found in this molecule.

Arabinose versus glucose: Despite only 92 genes being regulated, a mapping of these genes revealed that 13 of them were coding for putative polysaccharide-active gene products (App. Figure G.18) and all of them induced by arabinose. Interestingly, all three of the induced arabinan-acting genes were exo-acting arabinofuranosidases (EC 3.2.1.55), including *abfA* and *abfB*. However, the remaining induced genes constitute all of the activities of App. Table G.9, the xylan-acting genes, including β-galactosidase *lacA*, endo-xylanases and α-galacturonase A (*aguA*), suggesting that arabinose alone can induce the entire complex of xylan-degrading enzymes. This result is in line with the work by Yuan et al. (2006), where it was shown that the enzymes needed for degrading the complex polysaccharide inulin are induced by sucrose, but here a larger variation of genes induced by a more simple sugar is seen.

Starch versus xylan: A comparison of these two carbon sources is especially interesting, as no bond-types are shared between the two. Mapping of the significantly regulated genes (App. Figure G.19) indicates just this. The regulated genes are limited to all of the activities required to degrade starch (up-regulated on starch) and the activities required for degradation of xylan (up-regulated on xylan). Those up-regulated on starch include glucoamylase A (*glaA*), α-glucosidase A (*aglA/aglU*) as well as one or more of the three genes for α-amylase (*amyA*, *amyB* and gene ID 140567) with almost identical nucleotide-level sequences. It is not possible with an expression analysis to differentiate between them. The genes induced on xylan are the same genes as described to be induced by arabinose in the comparison of arabinose and glucose, with the exception that the endo-xylanase *xlnB* is induced on xylan instead of the putative endo-xylanase An15g04550/183088 that is induced by arabinose. We have thus identified a full set of extracellular polysaccharide-acting genes for the degradation of oat spelt xylan and starch and shown that with the exception of *xlnB*, arabinose induces the same array of xylan-degrading enzymes as does xylan.

9.1.3 Transcription-based clustering

To further investigate the regulation of single genes and the functions of genes that appear to be co-regulated, a clustering analysis of the expression indices of 161 putative and characterized glucoside hydrolases, polysaccharide lyases and carbohydrate esterases on the six different carbon sources was performed (Figure 9.2). 24 gene clusters were identified. Clustering allows the identification of genes that are only induced by the complex substrates, as well as genes that are induced equally well by a particular monosaccharide as well as the complex polysaccharide.

The transcription profile of each cluster (Fig-

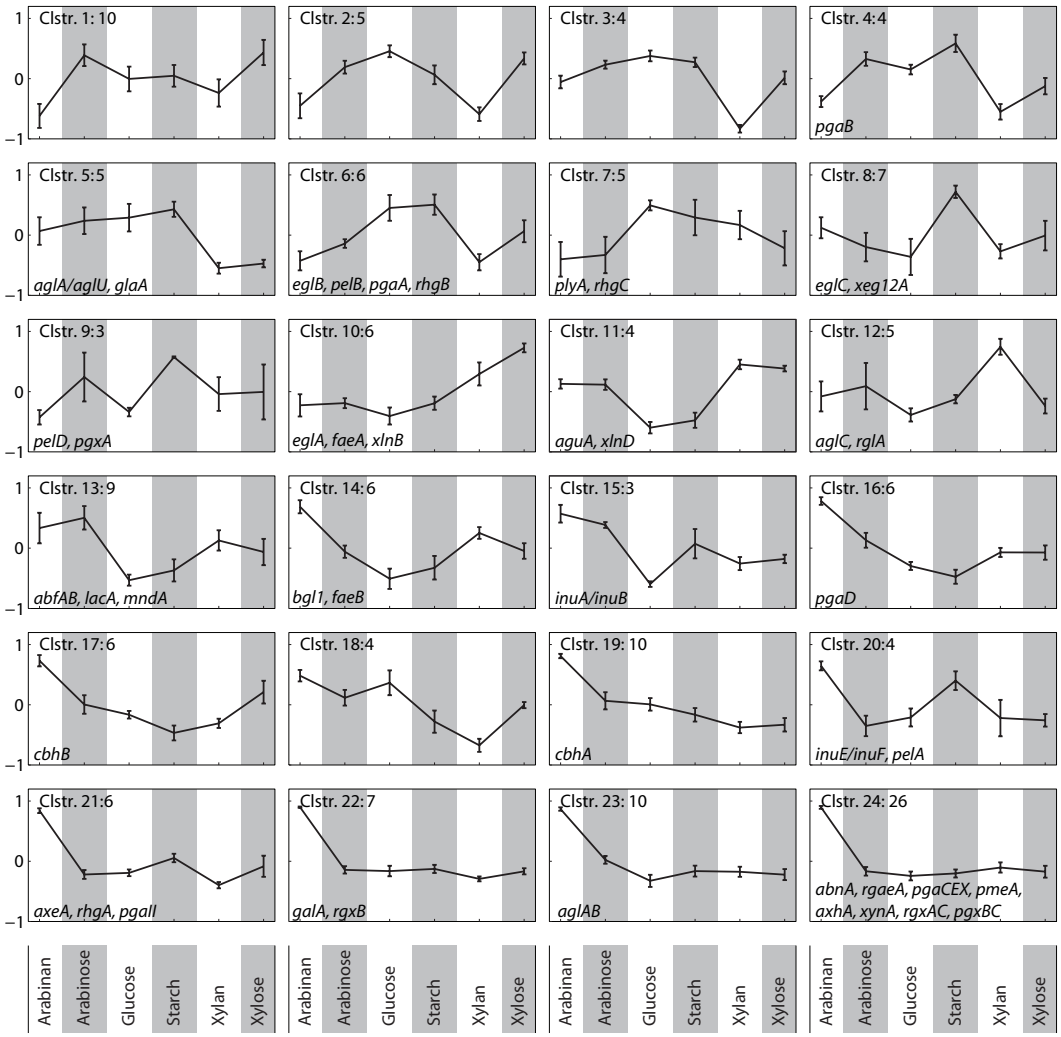

Figure 9.2: Clustering of 161 putative and characterized genes coding for polysaccharide-active enzymes according to expression profiles. The number of genes in each cluster is shown next to the cluster number. The gene names of known genes found in a particular cluster are found in each cluster. The genes were clustered using the ClusterLustre algorithm (Grotkjaer et al., 2006).

ure 9.2) was examined and classified in terms of regulation on the different carbon sources (App. Table G.18). If a distinct regulation was evident from the clustering profile, this information was added to the table as well, making this an overview of regulation and possible polysaccharide specificity for each of the 161 genes in the survey. The same study was made for the subset of genes coding for carbohydrate-active enzymes that were significantly regulated in one or more pairwise comparisons (App. Figure G.20 and App. Table G.19). This subset consists of 103 of the 161 genes, and 47 of the 57 characterized genes. However, as can be seen from App. Figure G.20, the clustering of the subset is very similar to those of the full set of genes (Figure 9.2). A comparison of the clusters of the two studies are also present in App. Table G.19. Since the majority of the genes were significantly regulated, and the remainder fall mostly in the same clusters, the following detailed analysis of the clustering was made using

the full set, thereby giving information on the expression patterns of as many genes as possible.

As it is evident from Figure 9.2, clusters 21–24 are highly similar. In making the clusters, it was attempted to use fewer clusters, and thereby combine these four clusters, however this combination required a decrease of the total numbers of clusters to 10, which increased the variation in the other clusters dramatically (Data not shown). For this reason, it was concluded that they have distinct patterns, as the small standard deviations of the clusters also suggest, and they have been kept as separate clusters. Furthermore, as clusters 21–24 are almost solely induced on arabinan, one would need to include more pectin-like substrates, e.g. polygalacturonic acid, in the analysis to be able to differentiate between the regulation of these genes. However, what one can conclude from this is that the genes of cluster 24 are specific for arabinan, and are not induced by any of the other saccharides in this study. It is interesting that *axhA* clusters with this group, as it was shown by van Peij et al. (1998a) to be induced on birchwood xylan but not on xylose. However, no induction on xylan is seen for cluster 24, suggesting that this gene is not induced by oat spelt xylan in this strain.

In examining the clusters for general trends, it was found that for most of the clusters, regulation on glucose and starch are very similar. This is in good agreement with the high level of free glucose in both cultures shown in Table 9.2. Exceptions are clusters 8, 9, 15, 18, and 20, which should be interesting for determining genes that are sensitive to degradation-products of starch, but not necessarily statistically significant in the comparison of starch versus glucose (Table 9.3).

By applying the mapping software described above, it is possible to describe the activity profile of a specific cluster. For each cluster, a map marking the genes of that cluster was prepared and examined to determine an activity profile if possible (All maps available from `www.computationalbiology.dk`, four examples present here).

Several of the clusters seems to be targeted to a specific type of polysaccharide. One example hereof is cluster 1. While it does not containing any characterized genes, the genes of the cluster are quite specifically predicted to code for enzymes with activity towards galactomannan and insoluble galactoglucomannan (App. Figure G.21). This homogeneity of functions confirms the putative annotations. As the cluster is up-regulated on the mono-sugars and the relatively easily degradable potato starch, it is likely that this cluster contains genes are induced by mono-sugar-abundance and code for a set of “scouting enzymes” with the role to liberate more substrates.

Cluster 5 has the highest level of expression on glucose and starch carbon sources. An examination of it with the enzyme mapping (App. Figure G.22), reveals that it constitutes a full set of co-regulated starch-degrading enzymes. The individual genes found in the cluster encode solely amylases and glucosidases, including glucoamylase A (*glaA*) and one or more of the three α-amylases with similar sequences discussed above (including *amyA* and *amyB*). The starch part of the map can be found in Figure 9.3. The fact that these enzymes cluster together can be seen as a validation of the transcription analysis and the clustering employed.

Rather interesting is the observation that the hemicellulose component arabinan seems to induce enzymes acting on cellulose and other β-glucans (App. Figure G.23–G.24)). This is seen in clusters 17 and 19, each containing one of the characterized cellobiohydrolases (which were shown to be induced on xylose by Gielkens et al. (1999)) and several putative β-glucosidases. β-glucans are not found as components of pectins, which makes this pattern a genuine induction across carbon-sources of entirely different chemical make-up.

As discussed above, the profile of cluster 24 indicates that it mainly contains genes that can be described as pectinolytic and a map-inspection (App. Figure G.25) confirms that these genes have a very distinct profile including all enzymatic activities for the degradation of rhamnogalacturonan I, smooth pectin and xylogalacturonan, all components of pectin, as are arabinan.

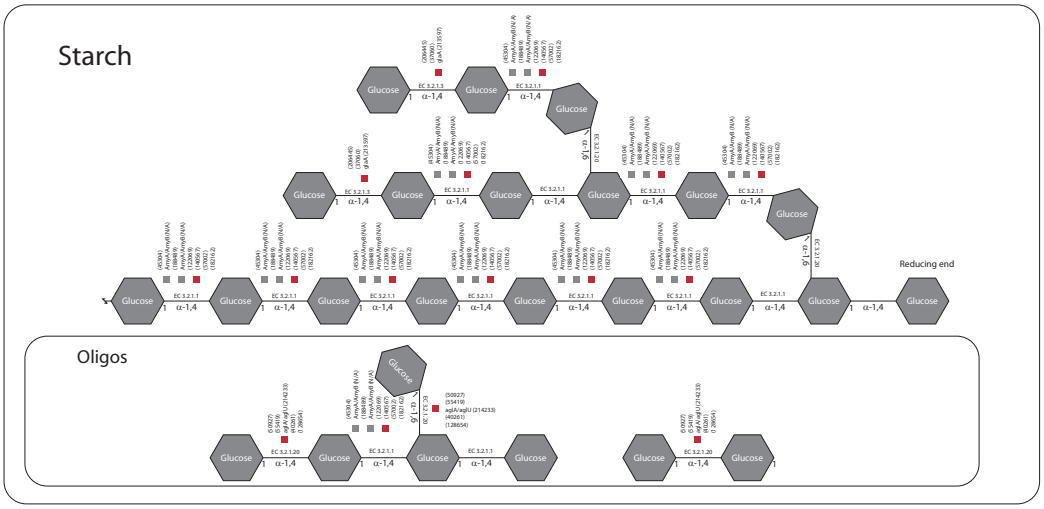

Figure 9.3: Map of starch-degrading enzymes in cluster 5. Genes marked with a red box are found in the cluster, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence.

9.1.4 Comparison of transcriptional regulation to previous studies

As described in the introduction, relatively few large-scale studies exist where the carbon source-based induction of extracellular enzymes have been studied. There is little overlap in the carbon sources employed in this study. Studies of polysaccharides have mainly been done with di-saccharides such as maltose or sucrose (Yuan et al., 2006) or on commercial preparations of pectin for food gelling (Martens-Uzunova et al., 2006, de Vries et al., 2002). However, a few have been made, which will be compared to the results of the present study here. A relatively larger number of studies including single or a few genes are published, however, these have been cited in the text above where appropriate, and in App. Tables G.1–G.16.

One study that is suitable for comparison is that of de Vries et al. (2002), where a principal component analysis (PCA) allows clustering according to expression profiles. While de Vries et al. (2002) focus mainly on pectinolysis, they include studies of growth on glucose, xylose, and arabinose. Their study describes *abfA*, *abfB* and *lacA* as being co-regulated and induced by 25 mM arabinose, which is in good accordance with the results of this chapter, as all of these are found in cluster 13. Interestingly however, de Vries et al. (2002) also reports *abnA* as being induced by arabinose and co-regulated with *abfAB* and *lacA*, but in the present work, only induction on arabinan is seen (cluster 24), and with a statistically significant up-regulation on arabinan in all pairwise comparisons. The PCA also indicates a close relationship between *pmeA*, *pgaX* and *abnA*, which describes accurately the patterns of cluster 24.

faeA and *faeB* are known to be largely co-regulated, but *faeA* is induced on xylose due to an induction by the xylanolytic regulator XlnR (van Peij et al., 1998a, de Vries et al., 2002). *faeA* and *faeB* are separated in clusters 10 and 14, that are very similar, but cluster 10 responds to xylose, whereas cluster 14 responds to the ferulic acid-containing arabinan, suggesting that *faeB* is more targeted to arabinan.

The work by Yuan et al. (2008b) examines induction of genes on xylose and maltose, which has an α-1,4-glucoside bond similar to starch. In Figure 2 in Yuan et al. (2008b), eleven genes can be seen to be induced by maltose and/or xylose (An11g03340, An04g06930, An01g06120, An14g04190, An12g02450, An09g03070, *agdA*, An01g10930, *glaA*, An09g05880, An09g03300).

All of these are regulated in a similar fashion in the present work, if maltose is seen to be similar to starch.

9.2 Conclusions

Enzyme preparations have multiple areas of application and are a billion dollar market with a low cost/profit ratio. Thus, it is of great importance and interest to gain an understanding of the processes leading to production of enzymes with a specific profile.

In this study, the first genome-scale characterization of all genes coding for carbohydrate-active enzymes identified in *A. niger* is provided. Based on a review of more than 190 articles and sequence database searches, information of 117 genes and enzymes has been systematized according to the poly-saccharide structures they degrade, thereby providing an updated reference on extracellular enzyme-expression in *A. niger*. This data-integration effort has produced schematic representations (maps) of 16 types of polysaccharide-structures, and integration with existing software allows for the plotting genome-scale data directly onto these maps.

An application of this knowledge was performed in a transcription study where statistical analysis as well as expression-level-based clustering and mapping were employed to provide transcription profiles of 161 genes on six defined carbon sources, thereby adding considerably to our knowledge of the transcription-level regulation of these genes. New knowledge was generated on the carbon source-based transcriptional regulation of previously characterized genes including, but not limited to, *abfA, abfB, aglA, cbhA, cbhB, glaA, eglA, eglB, faeA, faeB, lacA, pelA, pelB, pelC, xlnB* and *xynA* as well as more than 100 uncharacterized genes predicted to code for carbohydrate-active enzymes. The mapping of transcribed genes allowed us to identify induction by mono-saccharides of complete sets of enzymes for degradation of complex substrates, as well as the induction of cellulolytic enzymes on a hemicellulose substrate.

9.3 Materials and methods

9.3.1 Cultivation procedure

Strain information

The strain used was *A. niger* BO-1, a progenitor to high-yield amylase-producing industrial strains, obtained from Novozymes A/S. The strain is maintained as frozen spore suspensions at -80°C in 20 % glycerol.

Growth media

Complex medium: 2 g/L yeast extract, 3 g/L tryptone, 10 g/L glucose monohydrate, 20 g/L agar, 0.52 g/L KCl, 0.52 g/L $MgSO_4 \cdot 7H_2O$, 1.52 g/L KH_2PO_4 and 1 mL/L of trace elements solution. Trace element solution: 0.4 g/L $CuSO_4 \cdot 5H_2O$, 0.04 g/L $Na_2B_4O_7 \cdot 10H_2O$, 0.8 g/L $FeSO_4 \cdot 7H_2O$, 0.8 g/L $MnSO_4 \cdot H_2O$, 0.8 g/L $Na_2MoO_4 \cdot 2H_2O$, 8 g/L $ZnSO_4 \cdot 7H_2O$.

Batch cultivation medium salt concentrations: 2.5 g/L $(NH_4)_2SO_4$, 0.75 g/L KH_2PO_4, 1.0 g/L $MgSO_4 \cdot 7H_2O$, 1 g/L NaCl, 0.1 g/L $CaCl_2 \cdot 2H_2O$, 0.05 mL/L antifoam 204 (Sigma) and 1 mL/L trace element solution. Trace element solution composition: 7.2 g/L $ZnSO_4 \cdot 7H_2O$, 0.3 g/L $NiCl_2 \cdot 6H_2O$, 6.9 g/L $FeSO_4 \cdot 7H_2O$, 3.5 g/L $MnCl_2 \cdot 4H_2O$ and 1.3 g/L $CuSO_4 \cdot 5H_2O$. The carbon sources used for the cultivations were D-glucose$\cdot H_2O$ (20 g/L), D-xylose (20 g/L), L-arabinose (19.5 g/L + 0.5 g/L D-glucose), sugar beet arabinan (Megazyme, P-ARAB) (16.3 g/L), oat spelt xylan (Sigma, no 95590) (16.2 g/L) and potato starch (Sigma, no 85650) (16.5 g/L). These concentrations all equal 0.61 Cmole/L. Cultivations with L-arabinose were added D-glucose in order to make the spores germinate.

Sugar beet arabinan (Megazyme) is 95 % pure 1,5-α-L-arabinan containing arabinose:galactose:rhamnose:galacturonic acid in the ratios 88:4:2:6. The documentation further describes the arabinan as being “a polymer of 1,5-$alpha$-L-linked arabinofuranose units which is highly substituted by 1,3- and 1,2-linked single α-L-arabinofuranose residues. About 50 % of 1,5-linked arabinosyl residues in the main chain are substituted by 1,3 or 1,2 linked arabinofuranosyl branches.”

Oat spelt xylan (Sigma) contains $\leq$10 % arabinose, $\leq$15 % glucose, and $\geq$70 % xylose.

Shake flask cultivations

Shake flasks were initiated by spore inoculation to a final concentration of 2×10^9 spores/L. Spores were propagated on complex medium plates and incubated for 7–8 days at 30°C before being harvested with 10 mL of 0.01 % Tween 80. All cultivations were carried out in 500 mL baffled shake flasks with a total volume of 200 mL liquid medium at 30°C and 150 rpm. The initial pH was set to pH 2.5 to avoid pellet formation. The entire content of the shake flask was harvested when the biomass concentration was approximately half the maximum biomass concentration on the given medium (mid-growth phase). All cultivations were performed in biological triplicates except starch, where a duplicate culture was performed.

Sampling

Cell dry weight was determined using nitrocellulose filters (pore size 0.45 μm, Gelman Sciences). The filters were pre-dried in a microwave oven at 150 W for 15 minutes, cooled in a desiccator and subsequently weighed. A known volume of cell culture was filtered and the residue was washed with 0.9 % NaCl and dried on the filter for 15 minutes in a microwave oven at 150 W and cooled in a desiccator. The filtrate was saved for quantification of sugars and extracellular metabolites and stored at -80°C. The filter was weighed again and the cell mass concentration was calculated. These values were used to calculate maximum specific growth rates. For gene expression analysis, mycelium was harvested at the mid-late exponential phase (at approximately half the maximum concentration of biomass) by filtration through sterile Mira-Cloth (Calbiochem) and washed with a PBS buffer (8 g/L NaCl, 0.20 g/L KCl, 1.44 g/L Na_2HPO_4 and 0.24 g/L KH_2PO_4 in distilled water). The mycelium was quickly dried by squeezing, and subsequently frozen in liquid nitrogen. Samples were stored at -80°C until RNA extraction.

Quantification of sugars

The concentrations of sugar in the filtrates were determined using HPLC on an Aminex HPX-87H ion-exclusion column (BioRad, Hercules, CA). The column was eluted at 60°C with 5 mM H_2SO_4 at a flow rate of 0.6 mL/min. Sugars were detected with a refractive index detector and a UV detector.

9.3.2 Transcriptome analysis

Extraction of total RNA

40–50 mg of frozen mycelium was placed in a 2 mL Eppendorf tube, pre-cooled in liquid nitrogen, containing three steel balls (two balls with a diameter of 2 mm and one ball with a diameter of 5 mm). The tubes were then shaken in a Mixer Mill, at 5°C for 10 minutes, until the mycelium was ground to powder. Total RNA was isolated from the powder using the Qiagen RNeasy Mini Kit, according to the protocol for isolation of total RNA from plant and fungi. The quality of the extracted total RNA was assessed using a BioAnalyzer 2100 (Agilent Technologies Inc., Santa Clara, CA, USA) and the quantity determined using a spectrophotometer (GE Healthcare Bio-Sciences AB, Uppsala, Sweden). The total RNA was stored at -80°C until further processing.

Preparation of biotin-labeled cRNA and microarray processing

15 μg of fragmented biotin-labeled cRNA was prepared from 5 μg of total RNA and hybridized to the 3AspergDTU GeneChip (Andersen et al., 2008b) according to the Affymetrix GeneChip Expression Analysis Technical Manual (Aff, 2007).

cRNA was quantified in a spectrophotometer (same as above). cRNA quality was assessed using a BioAnalyzer. A GeneChip Fluidics Station FS-400 (fluidics protocol FS450_001) and a GeneChip Scanner 3000 were used for hybridization and scanning.

The scanned probe array images (.DAT files) were converted into .CEL files using the GeneChip Operating Software (Affymetrix).

Analysis of transcription data

Affymetrix CEL-data files were preprocessed using the statistical language and environment R (R Development Core Team, 2007) version 2.6.1. The probe intensities were normalized for background using the RMA method (Irizarry et al., 2003) using only perfect match (PM) probes. Normalization was performed subsequently using the quantiles algorithm (Bolstad et al., 2003). Gene expression values were calculated from the PM probes with the medianpolish summary method (Irizarry et al., 2003). All statistical preprocessing methods were used by invoking them through the affy package (Gautier et al., 2004).

Statistical analysis was applied to determine genes subject to differential transcriptional regulation. The limma package (Smyth, 2004) was used to perform moderated t-tests between two sets of triplicates from each pH level. Empirical Bayesian statistics were used to moderate the standard errors within each gene and Benjamini-Hochberg's method (Benjamini and Hochberg, 1995) to adjust for multi-testing. A cut-off value of adjusted $p<0.05$ was set to assess statistical significance.

Normalized and raw data-values are deposited with GEO as series GSE11930.

9.3.3 Clustering

Genes were clustered using the clustering algorithm ClustreLustre (Grotkjaer et al., 2006), using k-means normalization and accounting for biological replicates.

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Chapter 10

Conclusion

> "It is a far, far better thing that I do, that I have ever done; it is a far, far better rest that I go to that I have ever known"
> *Charles Dickens — A tale of two cities*

The focus in this thesis has been to study traits of Aspergilli relevant to biotechnology with the application of systems biology through new analytical and computational tools. The main contributions of the thesis are thus both the tools and the studies, wherein their applications are demonstrated, but the perspectives of the research reach beyond these.

The main tools provided are described in the work of chapters 3–6, the genome-scale metabolic model of *A. niger*, the ReMapper application and the tri-species *Aspergillus* DNA microarray for expression analysis. All of these have been applied — separately or in combination — in the studies presented in chapters 7–9. Furthermore, even though these tools were developed for the analysis of biotechnological applications, their design allows for applications that are not limited to the scope of this thesis, and may thus aid data interpretation in future systems biology studies.

While all of the individual studies of this thesis present interesting findings in their own right, the combined aspects of them show the potential and diversity of the applications of genome-scale techniques and systems biology to *Aspergillus* studies. First, these techniques are the most efficient way of conducting analyses of relevant processes that have systemic traits, e.g. the general study of organic acid production and gene expression profiles for all genes predicted to code for extracellular enzymes (chapters 8 and 9, respectively). As these studies demonstrate, systems biology allows the detection of patterns not previously described, even though these processes have been focus points of the *A. niger* research. Second, chapter 6 shows that knowledge can even be gained on a relatively well-described regulatory system such as the xylanolytic response regulator. Third, the work of chapter 7 has shown that even the production of a single product (glucoamylase or citric acid) has aspects that should be interpreted in a systems context, and the systemic impact of optimizing the yield of these productions is surprisingly large.

One reason for the high utility of genome-based analysis in the genus of *Aspergillus* may be that the genomes are relatively uncharted compared to well-studied model organisms such as *S. cerevisiae*, where a large amount of systems biology based research have been conducted. As the studies of this thesis show, context can be provided to uncharacterized genes, thus making sound hypotheses of function possible.

The work of this thesis has thus generated new tools, knowledge, functional annotation of genes, fresh hypotheses and a wealth of data that can be applied in developing current and new biotechnological processes. With the versatility demonstrated here, it thus is clear that even more can be learned from the application of systems biology to the study of Aspergilli in the future.

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Appendix A

Supplementaries for chapter 3

Table A.1: *Aspergillus niger* reconstructed metabolic network. Abbreviations of the names of the metabolites are found in Suppl. Table 2. For each reaction the following information is noted where it is known: The EC-number and enzyme name. A list of references discussing or indicating the presence of the reaction (If a reaction is found in another *Aspergillus sp* or inferred based on observations in *A. niger*, it will be written as Hondmann (1994, A. nidulans) or Morozova et al. (2002, Inferred) respectively). Gene numbers are from the *A. niger* CBS 513.88 and ATCC 1015-genome sequences (Columns CBS and ATCC respectively). The column named "Model" shows which other *Aspergillus* models the reaction is present in. ANID: *A. nidulans* iHD666, ANIG, *A. niger* iHD20, ANEW: The reaction is only present in *A. niger* iMA871. An $*$ indicates that an enzyme-complex catalyzes this reaction.

ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
Conversions								
NE1	:	DGLCe ⇆ 0.33 GLCe + 0.67 bDGLCe	Non enzymatic step	Non enzymatic reaction	David et al. (2003)	ANIG, ANID		
NE2	:	DGLC ⇆ 0.33 GLC + 0.67 bDGLC	Non enzymatic step	Non enzymatic reaction	Kinoshita et al. (1981)	ANIG, ANID		
r1	:	GLC ⇆ bDGLC	5.1.3.3	Aldose 1-epimerase	Kinoshita et al. (1981)	ANIG, ANID	An02g09090; An11g10890	55604; 56084
r2	:	GLAC ⇆ bGLAC	5.1.3.3	aldose-1-epimerase	Kinoshita et al. (1981)	ANEW	An02g09090; An11g10890	55604; 56084
r3	:	LARAB ⇆ bLARAB	5.1.3.3	aldose-1-epimerase	Kinoshita et al. (1981)	ANEW	An02g09090; An11g10890	55604; 56084
r4	:	bFRU ⇆ FRU	5.1.3.3	aldose-1-epimerase	Kinoshita et al. (1981)	ANEW	An02g09090; An11g10890	55604; 56084
Gluconeogenesis & Glycolysis								
Embden-Meyerhoff-Parnas Pathway								
r5	:	ATP + GLC ⇒ ADP + G6P	2.7.1.1	Hexokinase (hxk)	Jagannathan and Singh (1953), Muller (1986), Martinelli and Kinghorn (1994), Panneman et al. (1998), Alvarez-Vasquez et al. (2000), Karaffa et al. (2001)	ANIG, ANID	An02g14380; An06g00380; An13g00510	55651; 134301; 50817
r6	:	ATP + bDGLC ⇒ ADP + bDG6P	2.7.1.2	Glucokinase (glkA)	Panneman et al. (1996), Karaffa et al. (2001)	ANIG, ANID	An12g08610	201877
r7	:	G6P ⇆ F6P	5.3.1.9	Glucose-6-phosphate isomerase	Jagannathan and Singh (1953), Martinelli and Kinghorn (1994), Ruijter and Visser (1999), Alvarez-Vasquez et al. (2000)	ANIG, ANID	An16g05420	210433
r8	:	bDG6P ⇆ F6P	5.3.1.9	Glucose-6-phosphate isomerase	Jagannathan and Singh (1953), Ruijter and Visser (1999), Alvarez-Vasquez et al. (2000)	ANIG, ANID	An16g05420	210433
r9	:	G6P ⇆ bDG6P	5.3.1.9	Glucose-6-phosphate isomerase	Jagannathan and Singh (1953), Ruijter and Visser (1999), Alvarez-Vasquez et al. (2000)	ANIG, ANID	An16g05420	210433
r10	:	ATP + F6P ⇒ ADP + FDP	2.7.1.11	6-phosphofructokinase (Phosphofructokinase I, pfkA)	Jagannathan and Singh (1953), Habison et al. (1983), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000), Karaffa et al. (2001)	ANIG, ANID	An18g01670	54093
r11	:	FDP + H_2O ⇒ F6P + PI	3.1.3.11	Fructose-2,6-bisphosphatase	Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000)	ANIG, ANID	An04g05300	214375
r12	:	FDP ⇆ T3P2 + T3P1	4.1.2.13	Fructose-bisphosphate aldolase	Jagannathan and Singh (1953), Jagannathan et al. (1956), Muller (1986), Martinelli and Kinghorn (1994)	ANIG, ANID	An02g07470; An05g02040; An14g04410; An16g00110	55586; 43928; 211172; N/A
r13	:	T3P2 ⇆ T3P1	5.3.1.1	Triosephosphate isomerase (tpiA)	Inoue et al. (1988), Martinelli and Kinghorn (1994)	ANIG, ANID	An02g02920; An14g04920	206602; 56602
r14	:	T3P1 + PI + NAD ⇆ 13PDG + NADH	1.2.1.12	Glyceraldehyde 3-phosphate dehydrogenase (gpdA)	Muller (1986), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000)	ANIG, ANID	An16g01830	56485
r15	:	ADP + 13PDG ⇆ ATP + 3PG	2.7.2.3	Phosphoglycerate kinase	David et al. (2003)	ANIG, ANID	An08g02260	208318
r16	:	3PG ⇆ 2PG	5.4.2.1	Phosphoglycerate mutase	Jagannathan and Singh (1953), Muller (1986)	ANIG, ANID	An16g02990; An16g06010	210655; 40937
r17	:	2PG ⇆ PEP + H_2O	4.2.1.11	Phosphopyruvate hydratase (enolase)	Jagannathan and Singh (1953), Muller (1986), Martinelli and Kinghorn (1994)	ANIG, ANID	An18g06250	202692
r18	:	ADP + PEP ⇒ ATP + PYR	2.7.1.40	Pyruvate kinase (pkiA)	Patil and Ramakrishnan (1966), Perl (1982), Meixner-Monori et al. (1984), Muller (1986), Kubicek et al. (1988), de Graaff et al. (1992), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000)	ANIG, ANID	An07g08990	56137
r19	:	ATP + PYR + H_2O + CO_2 ⇒ ADP + PI + OA	6.4.1.1	Pyruvate carboxylase (pyc)	Tachibana (1964), Bercovitz et al. (1990), Martinelli and Kinghorn (1994), Jaklitsch et al. (1991), Pel et al. (2007)	ANIG, ANID	An04g02090	213185
r20	:	ATPm + PYRm + H_2Om + CO_2m ⇒ ADPm + PIm + OAm	6.4.1.1	Pyruvate carboxylase	Tachibana (1964), Ma et al. (1981), Bercovitz et al. (1990), Martinelli and Kinghorn (1994), Jaklitsch et al. (1991), Pel et al. (2007)	ANID	An15g02820	129399
r21	:	ATP + OA ⇒ ADP + PEP + CO_2	4.1.1.49	Phosphoenolpyruvate carboxykinase (ATP)	Woronick and Johnson (1960), Patil and Ramakrishnan (1966)	ANIG, ANID	An11g02550	208685
Pentose-Phosphate Shunt								

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r22	:	G6P + NADP ⇒ D6PGL + NADPH	1.1.1.49	Glucose 6-phosphate 1-dehydrogenase (gsdA)	McDonough and Martin (1958), Muller (1985), Jaklitsch et al. (1991), Wennekes et al. (1993), van den Broek et al. (1995), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000), Kirimura et al. (2000)	ANIG, ANID		An02g12140	55633
r23	:	D6PGL + H_2O ⇒ D6PGC	3.1.1.31	6-Phosphogluconolactonase	Martinelli and Kinghorn (1994)	ANIG, ANID		An01g05150	206051
r24	:	D6PGC + NADP ⇒ RL5P + CO_2 + NADPH	1.1.1.44	Phosphogluconate dehydrogenase (decarboxylating)	McDonough and Martin (1958), Muller (1985), Martinelli and Kinghorn (1994)	ANIG, ANID		An11g06120	178461
r25	:	RL5P ⇆ XUL5P	5.1.3.1	Ribulose-phosphate 3-epimerase	Martinelli and Kinghorn (1994), Muller (1985), de Groot et al. (2003)	ANIG, ANID		An09g03450	50154
r26	:	R5P ⇆ RL5P	5.3.1.6	Ribose-5-phosphate isomerase	Lakshminarayana et al. (1969b), Martinelli and Kinghorn (1994), Muller (1985), de Groot et al. (2003)	ANIG, ANID		An02g02930	206607
r27	:	R5P + XUL5P ⇆ S7P + T3P1	2.2.1.1	Transketolase	Martinelli and Kinghorn (1994), de Groot et al. (2003)	ANIG, ANID		An02g06430; An08g06570	197387; 207951
r28	:	E4P + XUL5P ⇆ F6P + T3P1	2.2.1.1	Transketolase	Martinelli and Kinghorn (1994), de Groot et al. (2003)	ANIG, ANID		An02g06430; An08g06570	197387; 207951
r29	:	S7P + T3P1 ⇆ E4P + F6P	2.2.1.2	Transaldolase	Martinelli and Kinghorn (1994), de Groot et al. (2003)	ANIG, ANID		An07g03160; An07g03850	40065; 209713
Tricarboxylic Acid Cycle									
r31	:	ACCOAm + H_2Om + OAm ⇆ CITm + COAm	2.3.3.1	Citrate synthase (citA)	Muller (1975b, 1986), Bercovitz et al. (1990), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000), Kubicek et al. (1988), Pel et al. (2007)	ANIG, ANID		An01g09940; An08g10920; An09g06680	35756; 176409; 202801
r32	:	CITm ⇆ ACOm + H_2Om	4.2.1.3	Aconitate hydratase	Muller (1975b), Neilson (1955), Muller (1986), Alvarez-Vasquez et al. (2000), Kirimura et al. (2000), Karaffa et al. (2001)	ANIG, ANID		An02g11040; An08g10530; An09g03870; An16g05760	130186; 52568; 212582; 48916
r33	:	ACOm + H_2Om ⇆ ICITm	4.2.1.3	Aconitate hydratase	Muller (1975b), Neilson (1955), Muller (1986), Alvarez-Vasquez et al. (2000), Kirimura et al. (2000), Karaffa et al. (2001)	ANIG, ANID		An02g11040; An08g10530; An09g03870; An16g05760	130186; 52568; 212582; 48916
r34	:	ICITm + NADPm ⇒ AKGm + CO_2m + NADPHm	1.1.1.42	Isocitrate dehydrogenase (*icdA*) ($NADP^+$)	Patil and Ramakrishnan (1966), Muller (1975b, 1986), Meixner-Monori et al. (1986), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000), Karaffa et al. (2001), Jaklitsch et al. (1991), Pel et al. (2007)	ANIG, ANID		An02g12430	47151
r30	:	ICITm + NADm ⇒ AKGm + CO_2m + NADHm	1.1.1.41	Isocitrate dehydrogenase (NAD+)	Muller (1975b), Jaklitsch et al. (1991), Pel et al. (2007)	ANIG, ANID	*	An08g05580; An18g06760	208051; 212289
r35	:	ICIT + NADP ⇒ AKG + CO_2 + NADPH	1.1.1.42	Isocitrate dehydrogenase ($NADP^+$)	Patil and Ramakrishnan (1966), Muller (1975b, 1986), Meixner-Monori et al. (1986), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000), Karaffa et al. (2001), Jaklitsch et al. (1991), Pel et al. (2007)	ANIG, ANID		An02g12430	47151
r36a	:	AKGm + TDPE1m ⇒ AKGE1m + CO_2m	1.2.4.2	α-ketoglutarate dehydrogenase	Muller (1975b), Meixner-Monori et al. (1985), Martinelli and Kinghorn (1994)	ANIG, ANID	*	An04g04750; An06g00390	212992; 47240
r36b	:	AKGE1m + LPSE2m ⇒ AKGE2m + TDPE1m	2.3.1.61	Dihydrolipoamide S-succinyl transferase	Meixner-Monori et al. (1985), Martinelli and Kinghorn (1994)	ANIG, ANID		An11g11280	56101
r36c	:	AKGE2m + COAm + NADm ⇆ LPSE2m + SUCCOAm + NADHm	1.8.1.4	Dihydrolipoamide dehydrogenase	Meixner-Monori et al. (1985), Martinelli and Kinghorn (1994)	ANIG, ANID		An07g06840	53232
r38	:	GDPm + PIm + SUCCOAm ⇆ GTPm + SUCCm + COAm	6.2.1.4	Succinate CoA ligase (GDP forming)	David et al. (2003)	ANIG, ANID	*	An08g02970; An08g02980	176118; 176118
r39	:	SUCCm + Qm ⇆ FUMm + QH_2m	1.3.5.1	Succinate dehydrogenase (ubiquinone)	Martinelli and Kinghorn (1994), Karaffa et al. (2001)	ANIG, ANID	*	An14g04395; An14g04400; An02g07600; An02g12770; An07g03170	201642; 201642; 130857; 55637; 40064
r40	:	FUMm + FADH2m ⇒ SUCCm + FADm	1.3.99.1	Succinate dehydrogenase	Muller (1975b), Kirimura et al. (2000), Karaffa et al. (2001)	ANIG, ANID		An01g13930; An02g05410	51710; 52233
r41	:	FUM + FADH2m ⇒ SUCC + FADm	1.3.99.1	Succinate dehydrogenase		ANID		An16g07150	205005
r42	:	FUMm + H_2Om ⇆ MALm	4.2.1.2	Fumarate hydratase	David et al. (2003)	ANIG, ANID		An12g07850	56673
r43	:	MAL ⇆ FUM + H_2O	4.2.1.2	Fumarate hydratase	Muller (1975a, 1986)	ANID		An12g07850	56673
r44	:	MALm + NADm ⇆ OAm + NADHm	1.1.1.37	Malate dehydrogenase	Muller (1975b), Ma et al. (1981), Bercovitz et al. (1990), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000), Karaffa et al. (2001), Pel et al. (2007)	ANIG, ANID		An16g00120	N/A

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r45	:	MAL + NAD ⇆ OA + NADH	1.1.1.37	Malate dehydrogenase	Muller (1975b), Ma et al. (1981), Muller (1986), Bercovitz et al. (1990), Jaklitsch et al. (1991), Martinelli and Kinghorn (1994), Alvarez-Vasquez et al. (2000), Karaffa et al. (2001), Pel et al. (2007)	ANIG, ANID		An11g07190; An15g00070; An12g00160	48047; 183145; 212768
Anaplerotic reactions (besides Gluconeogenesis)									
Glyoxylate Shunt					Martinelli and Kinghorn (1994)				
r46	:	ICITm ⇒ SUCCm + GLXm	4.1.3.1	Isocitrate lyase	Shah and Ramakrishnan (1963), Sahasrabudhe et al. (1986)	ANIG, ANID		An01g09270	196237
r47	:	ACCOAm + H_2Om + GLXm ⇒ MALm + COAm	4.1.3.2	Malate synthase	David et al. (2003)	ANIG, ANID		An15g01860	48680
Oxidation of malate to pyruvate									
r48c	:	MAL + NADP ⇒ PYR + CO_2 + NADPH	1.1.1.40	Malate dehydrogenase (NADP-specific) (malic enzyme)	Jernejc and Legisa (2002)	ANIG, ANID		An05g00930	211661
r48m	:	MALm + NADPm ⇒ PYRm + CO_2m + NADPHm	1.1.1.40	Malate dehydrogenase (NADP-specific) (malic enzyme)		ANID		An12g00160	212768
TCA intermediates metabolism									
r50	:	ATP + CIT + COA ⇒ ADP + PI + ACCOA + OA	2.3.3.8	ATP:citrate oxaloacetate-lyase ((pro-3S)-CH2COO- ->acetyl-CoA) (ATP-dephosphorylating)	Pel et al. (2007), Pfitzner et al. (1987)	ANIG, ANID		An11g00530	199043
r50m	:	ATPm + CITm + COAm ⇒ ADPm + PIm + ACCOAm + OAm	2.3.3.8	ATP:citrate oxaloacetate-lyase ((pro-3S)-CH2COO- ->acetyl-CoA) (ATP-dephosphorylating) mitochondrial	Pel et al. (2007), Pfitzner et al. (1987)	ANIG, ANID		An11g00510	208547
r37	:	CITm ⇒ OAm + ACm	4.1.3.6	Mitochondrial citrate lyase	Pel et al. (2007)	ANIG, ANID		An01g08610	51845
Oxalic acid					Rymowicz and Lenart (2003)				
r51	:	OA + H_2O ⇒ OXAL + AC	3.7.1.1	Oxaloacetate acetylhydrolase (oahA)	Muller (1975a), Lenz et al. (1976), Muller (1986), Kubicek et al. (1988), Ruijter and Visser (1999), Pedersen et al. (2000c), Hjort and Pedersen (2000)	ANIG, ANID		An10g00820	57241
r52	:	OXAL ⇒ FOR + CO_2	4.1.1.2	Oxalate decarboxylase	Emiliani and Riera (1968)	ANIG, ANID		An15g03980	182700
r56	:	OXALe ⇒ FORe + CO_2e	4.1.1.2	Oxalate decarboxylase		ANEW		An03g01140	214686
Methanol									
r53	:	METHOL + NAD ⇆ FALD + NADH	1.1.1.1	Alcohol dehydrogenase (adhA)	Lusta et al. (1991, A. terreus)	ANID		An12g09810; An17g01530; An01g12170; An01g14590; An02g02060; An02g02870; An03g01350; An04g02690; An08g09750; An09g03140; An11g04150; An11g04290; An12g09950; An13g00950; An13g03330; An14g02160; An14g07180; An16g00010; An16g00400; An16g06240	46038; 204476; 205557; 170152; 206534; 174157; 194416; 190222; 177276; 43351; 179042; 39027; 195091; 44729; 134944; N/A; 42017; 41439; 41421; 40925
Formic acid									
r54	:	FALD + NAD + H_2O ⇆ FOR + NADH	1.2.1.46	Formaldehyde dehydrogenase	Lusta et al. (1991, A. terrerus)	ANID		An10g00230	44975
r55	:	FOR + O_2 ⇒ H_2O_2 + CO_2	1.2.1.2	Formate oxidase	Hauge (1957)	ANEW		An15g00410	124156
r61	:	FALD + RGT + NAD ⇆ FGT + NADH	1.2.1.1	Formaldehyde dehydrogenase (glutathione)	Lusta et al. (1991, A. terreus)	ANID		An02g00080	173994
Pyruvate metabolism									
r56a	:	PYRm + LIPOm ⇒ ADHLIPOm + CO_2m	1.2.4.1	Pyruvate dehydrogenase (lipoamide)	Alvarez-Vasquez et al. (2000), Karaffa and Kubicek (2003), Pel et al. (2007)	ANIG, ANID	*	An01g00100; An07g09530; An11g04550	55510; 209315; 125186
r56b	:	COAm + ADHLIPOm + NADm ⇆ ACCOAm + LIPOm + NADHm	2.3.1.12	Dihydrolipoamide S-acetyltransferase and lipoamide dehydrogenase	Pel et al. (2007)	ANIG, ANID	*	An07g02180; An07g06840; An02g11910	53338; 53232; 197817

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r58	:	PYR ⇒ ACAL + CO_2	4.1.1.1	Pyruvate decarboxylase	David et al. (2003)	ANIG, ANID	An02g06820; An01g01590; An09g01030; An13g03320	55573; 125264 and 170782; 189097; 192165
r59	:	PYR + PI + O_2 + H_2O ⇒ ACTP + CO_2 + H_2O_2	1.2.3.3	Pyruvate oxidase	Patil and Ramakrishnan (1966)	ANEW		
r60	:	ATP + AC ⇒ ADP + ACTP	2.7.2.1	Acetate kinase	Pel et al. (2007)	ANIG, ANID	An02g06420	206885
Methylglyoxal bypass								
r62	:	T3P2 ⇒ MTHGXL + PI	4.2.3.3	Methylglyoxal synthase or non-enzymatic	Martinelli and Kinghorn (1994)	ANIG		
r63	:	T3P1 ⇒ MTHGXL + PI	No EC	chemical reaction	Martinelli and Kinghorn (1994)	ANEW		
r64	:	MTHGXL + NADPH ⇆ LACAL + NADP	1.1.1.78	D-Lactaldehyde dehydrogenase (Methylglyoxal reductase) (MGR I)	Inoue et al. (1988), Martinelli and Kinghorn (1994)	ANIG, ANID		
r65	:	LACAL + NAD + H_2O ⇒ LAC + NADH	1.2.1.22	Lactaldehyde dehydrogenase	Inoue et al. (1988)	ANIG, ANID		
r66	:	LAC + NAD ⇆ PYR + NADH	1.1.1.28	D-lactate dehydrogenase	David et al. (2003)	ANIG	An01g09780	51812
r67	:	RGT + MTHGXL ⇆ LGT	4.4.1.5	Lactoylglutathione lyase (glyoxylase I)	Inoue et al. (1987, 1988), Martinelli and Kinghorn (1994)	ANIG, ANID	An08g09300; An11g02860; An02g05670	37996; 38904; 52241
r68	:	LGT + H_2O ⇒ LAC + RGT	3.1.2.6	Hydroxyacylglutathione hydrolase (glyoxylase II)	Inoue et al. (1988)	ANIG, ANID	An04g07220; An11g07320; An14g06340	214187; 48052; 184532
Methylcitrate pathway					Sealy-Lewis and Fairhurst (1998), Kanehisa et al. (2002)			
r69	:	PROPAL + NAD + H_2O ⇆ PROP + NADH	1.2.1.3	Aldehyde dehydrogenase (NAD+)	Kazimirova and Novotelnov (1956)	ANEW	An04g03400; An01g15170; An08g07290; An08g10820; An10g00850; An15g05890; An18g04130	57028; N/A; 55742; 37719; 57243; 40734; 187856
r70	:	ATPm + PROPm + COAm ⇆ AMPm + PPIm + PROPCOAm	6.2.1.17	Propanoate:CoA ligase (AMP-forming)	Sealy-Lewis and Fairhurst (1998)	ANIG, ANID		
r85	:	ATP + PROP + COA ⇆ AMP + PPI + PROPCOA	6.2.1.17	Propanoate:CoA ligase (AMP-forming)	Sealy-Lewis and Fairhurst (1998)	ANEW		
r71	:	PROPCOAm + H_2Om + OAm ⇆ 2MCITm + COAm	2.3.3.5	2-Methylcitrate synthase	Miyakoshi et al. (1987), Sealy-Lewis and Fairhurst (1998)	ANIG, ANID	An15g01920	48684
r72	:	2MCITm ⇆ 2MACOm + H_2Om	4.2.1.79	2-methylcitrate hydrolyase	Sealy-Lewis and Fairhurst (1998, Inferred)	ANIG	An15g01780	53423
r73	:	2MACOm + H_2Om ⇆ 2MICITm	4.2.1.99	2-methylisocitrate dehydratase	Sealy-Lewis and Fairhurst (1998, Inferred)	ANIG		
r74	:	2MICITm ⇆ PYRm + SUCCm	4.1.3.30	2-methylisocitrate lyase	Miyakoshi et al. (1987)	ANIG	An12g07630	42171
4-aminobutyrate (GABA) shunt								
r75	:	GLUm ⇒ GABAm + CO_2m	4.1.1.15	Glutamate decarboxylase	Kumar et al. (2000c)	ANID	An02g06860; An08g08840; An15g04770	173821; 52600; 210245
r76	:	GABAm + AKGm ⇒ SUCCSALm + GLUm	2.6.1.19	4-Aminobutyrate transaminase	David et al. (2003)	ANIG, ANID	An17g00910	57265
r77	:	SUCCSALm + NADm + H_2Om ⇒ SUCCm + NADHm	1.2.1.16	Succinate-semialdehyde dehydrogenase (NAD(P)+)	Kumar and Punekar (1998)	ANIG, ANID	An15g01740; An04g02610; An14g02870	56305; 57046; 56568
ONE CARBON -METABOLISM								
Folate biosynthesis								
r78	:	GTP + 2 H_2O ⇒ FOR + AHTD	3.5.4.16	GTP cyclohydrolase I	Cossins and Chen (1997, Inferred)	ANID	An09g05310	212481
r79	:	AHTD ⇒ DHP + 3 PI	3.1.3.1	Glycerophosphatase, alkaline phosphatase; nucleoside triphosphatase	Rama and Shanmugasundaram (1985, A. nidulans)	ANID	An07g07520	209506
r80	:	DHP ⇒ AHHMP + GLAL	4.1.2.25	Dihydroneopterin aldolase		ANID	An16g03880	49007
r991	:	GLAL + NAD + H_2O ⇆ GLYA + NADH	1.2.1.21	Glycolaldehyde dehydrogenase		ANEW		
r992	:	GLYA + O_2 ⇒ GLX + H_2O_2	1.1.3.15	Glycolate oxidase		ANEW	An01g14530; An12g10140	46259; 46010
r81	:	AHHMP + ATP ⇒ AMP + AHHMD	2.7.6.3	6-Hydroxymethyl-7,8 dihydropterin pyrophosphokinase		ANID	An16g05350	183733
r82	:	CHOR + GLN ⇒ ADCHOR + GLU	6.3.5.8	Aminodeoxychorismate synthase		ANID		
r83	:	ADCHOR ⇒ PYR + PABA	4.1.3.38	Aminodeoxychorismate lyase		ANID		
r84	:	PABA + AHHMD ⇒ PPI + DHPT	2.5.1.15	Dihydropteroate synthase	Cossins and Chen (1997, Inferred)	ANID	An16g03880	49007
r86	:	DHPT + ATP + GLU ⇒ ADP + PI + DHF	6.3.2.12	Dihydrofolate synthase	Iwai et al. (1977)	ANID		

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r87	:	DHF + NADPH ⇒ NADP + THF	1.5.1.5	Dihydrofolate reductase	Balinska and Paszewski (1979, A. nidulans)	ANIG, ANID	An02g12420	47150
r88	:	THF + ATP + GLU ⇆ ADP + PI + THFG	6.3.2.17	Tetrahydrofolylpolyglutamate synthase	Lewandowska et al. (1996, A. nidulans)	ANID	An02g02950; An04g01120; An04g02490; An04g09750	174911; 50605; 54580; 122883
Folate one-carbon pool					Cossins and Chen (1997), Kanehisa et al. (2002)			
r89	:	ATPm + FORm + THFm ⇒ ADPm + PIm + FTHFm	6.3.4.3	Formate-dihydrofolate ligase (10-Formyltetrahydrofolate synthetase, FTHFS) (Trifunctional)	Cossins and Chen (1997, Inferred)	ANID	An02g12420	47150
r90	:	FTHFm ⇆ METHFm + H_2Om	3.5.4.9	Methenyltetrahydrofolate cyclohydrolase (Trifunctional)	Cossins and Chen (1997, Inferred)	ANID	An02g12420	47150
r91	:	METHFm + NADPHm + Hm ⇆ METTHFm + NADPm	1.5.1.5	Methylenetetrahydrofolate dehydrogenase ($NADP^+$) (Trifunctional)	Cossins and Chen (1997, Inferred)	ANID	An02g12420	47150
r92	:	METTHFm + NADPHm + Hm ⇒ MTHFm + NADPm	1.5.1.20	Methylenetetrahydrofolate reductase (NADPH)		ANID	An02g03270	55539
r93	:	METTHF + NAD ⇒ METHF + NADH	1.5.1.15	Methylenetetrahydrofolate dehydrogenase (NAD+)	Lewandowska et al. (1996, A. nidulans)	ANID	An16g07400	214561
r94	:	METHF + H_2O ⇆ FTHF	3.5.4.9	Methenyltetrahydrofolate cyclohydrolase		ANID	An02g12420	47150
r95	:	FTHF + H_2O ⇒ FOR + THF	3.5.1.10	5-formyltetrahydrofolate deformylase		ANEW	An01g11650	196101
r96	:	METTHF + NADPH ⇒ MTHF + NADP	1.5.1.20	Methylenetetrahydrofolate reductase (NADPH)	Balinska and Paszewski (1979, A. nidulans)	ANIG	An09g05860	50057
Coenzyme A and pantothenate biosynthesis								
r97	:	OIVALm + METTHF + H_2O ⇒ AKP + THF	2.1.2.11	Ketopentoate hydroxymethyl transferase		ANID		
r98	:	AKP + NADPH ⇒ NADP + PANT	1.1.1.169	Ketopantoate reductase (2-dehydropantoate 2-reductase)		ANID	An09g01130; An18g01140; An11g09950	56955; 42642; 178804
r99	:	AKPm + NADPHm ⇒ NADPm + PANTm	1.1.1.169	Ketopantoate reductase (2-dehydropantoate 2-reductase)		ANID	An09g01130; An11g09950	56955; 178804
r100	:	PANT + bALA + ATP ⇒ AMP + PPI + PNTO	6.3.2.1	Pantoate-B-alanine ligase	Shimizu et al. (1974)	ANID	An18g01970	49810
r101	:	PNTO + ATP ⇒ ADP + 4PPNTO	2.7.1.33	Pantothenate kinase	Shimizu et al. (1974)	ANID	An02g13550	37546
r102	:	4PPNTO + CTP + CYS ⇒ CMP + PPI + 4PPNCYS	6.3.2.5	Phosphopantothenate-cysteine ligase	Shimizu et al. (1974)	ANID		
r103	:	4PPNCYS ⇒ CO_2 + 4PPNTE	4.1.1.36	Phosphopantothenate-cysteine decarboxylase	Shimizu et al. (1974)	ANID		
r104	:	4PPNTE + ATP ⇒ PPI + DPCOA	2.7.7.3	Phospho-pantethiene adenylyltransferase (Bifunctional with 2.7.1.24)	Shimizu et al. (1974)	ANID		
r105	:	DPCOA + ATP ⇒ ADP + COA	2.7.1.24	DephosphoCoA kinase (Bifunctional with 2.7.7.3)	Shimizu et al. (1974)	ANID		
Biotin biosynthesis					Parry and Kunitani (1979), Parry and Naidu (1980)			
r107	:	3 MALCOA + 4 NADPH ⇒ 4 NADP + CHCOA + 2 CO_2 + 2 COA + 2 H_2O	6.4.1.2; 6.3.4.1; 4 2.3.1.85;1.1.1.10(	B-ketoacyl-ACP synthase (c10,0), fatty acyl CoA synthase	Parry and Naidu (1980, Inferred)	ANEW		
r108	:	ALA + CHCOA ⇆ CO_2 + COA + AONA	2.3.1.47	8-Amino-7-oxononanoate synthase	Parry and Naidu (1980, Inferred)	ANID	An04g01140; An11g05560; An12g00920; An15g01980	190614; 179151; 189889; 200589
r109	:	AONA + SAM ⇆ DAONA + SAMOB	2.6.1.62	adenosyl:methionine-8-amino-7-oxononanoate aminotransferase	Parry and Naidu (1980, Inferred)	ANEW	An15g01990	48688
r110	:	DAONA + ATP + CO_2 ⇆ ADP + PI + DTB	6.3.3.3	dethiobiotin synthetase	Parry and Naidu (1980, Inferred)	ANEW		
r111	:	DTB + S ⇆ BT	2.8.1.6	Biotin synthase	Tepper et al. (1966), Parry and Kunitani (1979), Parry and Naidu (1980)	ANID	An15g02000	51633
OTHER CARBOHYDRATES, ALCOHOLS AND ORGANIC ACIDS								
C_2 METABOLISM								
Acetate/Acetaldehyde/Ethanol metabolism					Martinelli and Kinghorn (1994)			

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r113	:	ETH + NAD ⇆ ACAL + NADH	1.1.1.1	Alcohol dehydrogenase (adhA)	Martinelli and Kinghorn (1994)	ANIG, ANID	An12g09810; An17g01530; An01g12170; An01g14590; An02g02060; An02g02870; An03g01350; An04g02690; An08g09750; An09g03140; An11g04150; An11g04290; An12g09950; An13g00950; An13g03330; An14g02160; An14g07180; An16g00010; An16g00400; An16g06240	46038; 204476; 205557; 170152; 206534; 174157; 194416; 190222; 177276; 43351; 179042; 39027; 195091; 44729; 134944; N/A; 42017; 41439; 41421; 40925
r114	:	ETH + NADP ⇆ ACAL + NADPH	1.1.1.2	Alcohol dehydrogenase (Catalyzed by Glycerol dehydrogenase II ($NADP^+$) EC 1.1.1.72)	David et al. (2003)	ANIG	An05g02070; An10g00010; An16g02510	190030; N/A; 184073
r115	:	ACAL + NAD + H_2O ⇒ AC + NADH	1.2.1.3	Aldehyde dehydrogenase (NAD+) (aldA)	O'Connell and Kelly (1988, 1989, 1992), Martinelli and Kinghorn (1994)	ANIG, ANID	An04g03400; An01g15170; An08g07290; An08g10820; An10g00850; An15g05890; An18g04130	57028; N/A; 55742; 37719; 57243; 40734; 187856
r116	:	AC + COA + ATP ⇒ AMP + PPI + ACCOA	6.2.1.1	Acetyl-CoA synthase (acuA)	Sealy-Lewis and Fairhurst (1998)	ANIG, ANID	An04g05620	214348
r117	:	ACCOA + H_2O ⇒ COA + AC	3.1.2.1	Acetyl-CoA hydrolase	Ramakrishnan and Raina (1958), Ramakrishnan et al. (1959)	ANIG, ANID	An16g07110	214587
r118	:	ETHm + NADm ⇆ ACALm + NADHm	1.1.1.1	Alcohol dehydrogenase		ANID	An12g09810; An17g01530; An01g12170; An01g14590; An02g02060; An02g02870; An03g01350; An04g02690; An08g09750; An09g03140; An11g04150; An11g04290; An12g09950; An13g00950; An13g03330; An14g02160; An14g07180; An16g00010; An16g00400; An16g06240	46038; 204476; 205557; 170152; 206534; 174157; 194416; 190222; 177276; 43351; 179042; 39027; 195091; 44729; 134944; N/A; 42017; 41439; 41421; 40925
r119	:	ACALm + NADm + H_2Om ⇒ ACm + NADHm	1.2.1.3	Aldehyde dehydrogenase (NAD+) (adhA)		ANID	An04g03400; An01g15170; An08g07290; An08g10820; An10g00850; An15g05890; An18g04130	57028; N/A; 55742; 37719; 57243; 40734; 187856
r120	:	ACm + COAm + ATPm ⇒ AMPm + PPIm + ACCOAm	6.2.1.1	Acetyl-CoA synthase	Pel et al. (2007)	ANIG, ANID	An05g00390	185892
r121	:	ACCOAm + H_2Om ⇒ COAm + ACm	3.1.2.1	Acetyl-CoA hydrolase	David et al. (2003)	ANIG, ANID	An16g07110	214587
C_3 METABOLISM								
Glycerol metabolism								

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r122	:	GL + NAD ⇒ GLYN + NADH	1.1.1.6	Glycerol dehydrogenase	Martinelli and Kinghorn (1994)	ANIG, ANID	An01g06970	196413
r123	:	GL + O_2 ⇒ GLYAL + H_2O_2	1.1.3.13	Alcohol oxidase		ANID	An15g02200; An18g05480	56311; 42956
r124	:	GLYAL + NADPH ⇒ GL + NADP	1.1.1.72	Glycerol dehydrogenase	Jennings (1984), Schuurink et al. (1990), Martinelli and Kinghorn (1994)	ANIG, ANID	An01g06970	196413
r126	:	GL + O_2 ⇒ GLYN + H_2O_2	1.1.3.13	Alcohol oxidase		ANID	An15g02200; An18g05480	56311; 42956
r127	:	GL + NADP ⇒ GLYN + NADPH	1.1.1.72	Glycerol dehydrogenase ($NADP^+$)	Baliga et al. (1964), Schuurink et al. (1990)	ANEW	An01g06970	196413
r128	:	GL + ATP ⇒ GL3P + ADP	2.7.1.30	Glycerol kinase	Witteveen et al. (1990a), Witteveen and Visser (1995)	ANIG, ANID	An04g04890	45434
r129	:	GL3P + FADm ⇒ T3P2 + FADH2m	1.1.99.5	Glycerol 3-phosphate dehydrogenase (FAD dependent) (FAD-dependent sn-glycerol-3-phosphate dehydrogenase)	Witteveen et al. (1990a)	ANIG, ANID	An08g00210	55910
r130	:	GLYN + ATP ⇒ T3P2 + ADP	2.7.1.29	Glycerone kinase	Witteveen et al. (1990a)	ANIG, ANID	An14g06500	56628
r131	:	T3P2 + NADH ⇒ GL3P + NAD	1.1.1.8	Glycerol 3-phosphate dehydrogenase (NAD+ dependent)	David et al. (2003)	ANIG, ANID	An15g07390	48886
r132	:	GL3P + H_2O ⇒ GL + PI	3.1.3.21	Glycerol 3-phosphate phosphatase	David et al. (2003)	ANIG, ANID	An08g02530	176581
Glycerate metabolism								
r133	:	G + NADP ⇆ 3HPYR + NADPH	1.1.1.29	glycerate dehydrogenase	Behal and Hamilton (1962), Behal (1967)	ANEW	An08g06710	207936
L-lactate								
r183	:	LLAC + NAD ⇒ PYR + NADH	1.1.1.27	L-Lactate dehydrogenase	David et al. (2003)	ANIG, ANID	An04g08220	137087
C_4 METABOLISM								
Tartrate metabolism								
r134	:	TAR + NAD ⇆ OXGLY + NADH	1.1.1.93	Tartrate dehydrogenase	David et al. (2003)	ANIG, ANID	An01g03030	171830
r135	:	TAR ⇆ OA + H_2O	4.2.1.32	Tartrate dehydratase	Patil and Ramakrishnan (1966)	ANEW		
D-Erythrose/Erythritol metabolism								
r136	:	E + NADPH ⇒ EOL + NADP	1.1.1.72	Glycerol dehydrogenase	Schuurink et al. (1990)	ANIG, ANID	An01g06970	196413
r138	:	E + ATP ⇒ E4P + ADP		Erythrulose kinase	David et al. (2003), Hondmann (1994, A. nidulans)	ANIG		
r139	:	E4P + H_2O ⇒ PI + E		Erythrose 4-phosphate phosphatase	David et al. (2003), Hondmann (1994, A. nidulans)	ANIG		
r140	:	EOL + NAD ⇒ E + NADH		Erythrose reductase	David et al. (2003), Hondmann (1994, A. nidulans)	ANIG		
r141	:	EOL + NAD ⇒ EU + NADH		Erythrose dehydrogenase	David et al. (2003), Hondmann (1994, A. nidulans)	ANIG		
r142	:	EU + ATP ⇒ EU1P + ADP		Erythrulose kinase	David et al. (2003), Hondmann (1994, A. nidulans)	ANIG		
r143	:	EU1P ⇒ T3P1 + FALD	4.1.2.2	Ketotetrose-phosphate aldolase	David et al. (2003), Hondmann (1994, A. nidulans)	ANIG		
C_5 METABOLISM								
L-Arabinose/Arabitol metabolism					Witteveen et al. (1989)			
r144	:	LAOL + NADP ⇆ LARAB + NADPH	1.1.1.21	L-arabinose reductase	Witteveen et al. (1989), Martinelli and Kinghorn (1994), vanKuyk et al. (2001), de Groot et al. (2003), de Groot et al. (2005)	ANIG	An01g14880; An16g01720	46249; 53686
r145	:	LAOL + NAD ⇆ LXUL + NADH	1.1.1.12	L-Arabitol dehydrogenase	Witteveen et al. (1989), Martinelli and Kinghorn (1994), vanKuyk et al. (2001), de Groot et al. (2003), de Groot et al. (2005)	ANIG, ANID	An01g10920	46405
r146	:	LXUL + NADPH ⇆ XOL + NADP	1.1.1.10	L-Xylulose reductase	Martinelli and Kinghorn (1994), vanKuyk et al. (2001), de Groot et al. (2003), Witteveen et al. (1989, 1994)	ANIG, ANID	An11g03260	47908
D-Xylose/D,L-Xylulose/Xylitol metabolism					Witteveen et al. (1994), de Groot et al. (2003)			
r147	:	XYL + NADPH ⇆ XOL + NADP	1.1.1.21	D-Xylose reductase (xyrA) (xylitol dehydrogenase)	Witteveen et al. (1989), Martinelli and Kinghorn (1994), Witteveen et al. (1994), vanKuyk et al. (2001), Hasper et al. (2002), de Groot et al. (2003), de Groot et al. (2005)	ANIG, ANID	An01g03740	51997
r148	:	XOL + NADP ⇒ XUL + NADPH	1.1.1.10	xylitol dehydrogenase		ANIG, ANID	An11g03260	47908
r149	:	XOL + NAD ⇒ XUL + NADH	1.1.1.9	D-Xylulose reductase (xylitol dehydrogenase)	Witteveen et al. (1989), Martinelli and Kinghorn (1994), Witteveen et al. (1994), de Groot et al. (2003), vanKuyk et al. (2001)	ANIG, ANID	An05g02260; An07g01320; An08g09380; An12g00030; An15g04610	212968; N/A; 37988; 203198; 48775
D-arabinose metabolism					Witteveen et al. (1989)			
r150	:	ARABLAC + NADPH ⇆ ARAB + NADP	1.1.1.117	D-Arabinose 1-dehydrogenase [NAD(P)+]	Witteveen et al. (1989)	ANID	An01g06970	196413

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r151	:	ARAB + NADPH ⇆ AOL + NADP	1.1.1.21	Aldehyde reductase	Witteveen et al. (1989, 1994)	ANIG	An01g14880; An16g01720	46249; 53686
r152	:	AOL + NAD ⇒ XUL + NADH	1.1.1.11	D-arabitol dehydrogenase	Witteveen et al. (1989, 1994), vanKuyk et al. (2001)	ANIG, ANID	An04g09410	51398
r153	:	AOL + NADP ⇒ XUL + NADPH	1.1.1.11	D-arabitol dehydrogenase	Witteveen et al. (1989), vanKuyk et al. (2001)	ANIG, ANID	An04g09410	51398
Xylulose								
r154	:	ATP + XUL ⇒ ADP + XUL5P	2.7.1.17	Xylulose kinase	Witteveen et al. (1989, 1994), Martinelli and Kinghorn (1994), vanKuyk et al. (2001), de Groot et al. (2003)	ANIG, ANID	An07g03140	209771
r155	:	XUL5P + FALD ⇆ T3P1 + GLYN	2.2.1.3	Dihydroxyacetone synthase	Lusta et al. (1991, A. terrerus)	ANID	An14g03500	184680
Ribose								
r156	:	ATP + RIB ⇒ ADP + R5P	2.7.1.15	Ribokinase	David et al. (2003)	ANIG, ANID	An15g07500	40855
r157	:	R5P ⇆ R1P	5.4.2.2	Phosphoglucomutase	Khanna and Tewari (1963)	ANID	An02g07650	55590
r158	:	RIB + NADPH ⇆ RIBOL + NADP	1.1.1.21	D-Ribose reductase	Witteveen et al. (1989)	ANIG	An01g14880; An16g01720	46249; 53686
r159	:	RIBOL + NAD ⇒ RL + NADH	1.1.1.56	Ribitol dehydrogenase	Witteveen et al. (1989)	ANIG	An13g02310; An18g00010	192184; 42574
r160	:	RIBOL + NADP ⇒ RL + NADPH	1.1.1.56	Ribitol dehydrogenase	Witteveen et al. (1989)	ANIG	An13g02310; An18g00010	192184; 42574
Ribulose								
r161	:	ATP + RL ⇒ ADP + RL5P	2.7.1.47	Ribulokinase		ANID	An14g00160	53716
r162	:	RL + NADPH ⇒ AOL + NADP	No EC	ribulose reductase	Hondmann (1994, A.nidulans), Morozova et al. (2002, Inferred)	ANEW		
C_6 METABOLISM								
Gluconic acid/Gluconate metabolism								
r163	:	bDGLCe + O_2e ⇆ GLCN15LACe + H_2O_2e	1.1.3.4	Glucose oxidase (goxC)	Muller (1977), Frederick et al. (1990), Martinelli and Kinghorn (1994), Witteveen et al. (1992), Kim et al. (2001), Leskovac et al. (2005)	ANIG, ANID	An12g03430; An12g03440; An01g14740; An07g00450	50376; 50376; 55227; 40254
r164	:	bDGLC + O_2 ⇆ GLCN15LAC + H_2O_2	1.1.3.4	Glucose oxidase (god)	Muller (1977), Frederick et al. (1990), Martinelli and Kinghorn (1994), Witteveen et al. (1992), Kim et al. (2001), Leskovac et al. (2005), Bhatti et al. (2006)	ANID	An12g03430; An12g03440; An01g14740; An07g00450	50376; 50376; 55227; 40254
r165	:	GLCN15LACe + H_2Oe ⇒ GLCNTe	3.1.1.17	Gluconolactonase (lactonase)	Witteveen et al. (1992, 1993), Ogawa et al. (2002)	ANIG, ANID	An12g01570	N/A
NE6	:	GLCN15LAC + H_2O ⇒ GLCNT	No EC	Spontaneous reaction or catalyzed by glucose oxidase	Bhatti et al. (2006)	ANIG, ANID		
r166	:	D6PGC + H_2O ⇒ GLCNT + PI	3.1.3.1	Alkaline phosphatase	Ramaswamy and Bheemeswar (1976), Muller (1977), Rokosu and Uadia (1980), Karaffa et al. (2001)	ANIG, ANID	An07g07520; An18g04040	209506; 42852
r167	:	D6PGC + H_2O ⇒ GLCNT + PI	3.1.3.2	Acid phosphatase (aphA)	Muller (1977), Wyss et al. (1998)	ANIG, ANID	An14g02650; An08g09850; An09g00310; An12g10630; An13g01750; An14g01550; An16g01730; An16g09130; An18g04140	49304; 52587; 43568; 51468; 57215; 56545; 183355; 193642; 42861
r169	:	GLCNT + ATP ⇒ D6PGC + ADP	2.7.1.12	Gluconokinase	Lakshminarayana et al. (1969b), Muller (1986)	ANIG	An01g07300; An01g14850	127436; 170633
r168	:	D6PGC + NADP ⇆ D6PDGC + NADPH	1.1.1.43	6-phosphogluconate dehydrogenase	Lakshminarayana et al. (1969b,c), Muller (1986)	ANEW	An11g02040	199133
r170	:	GLCNT ⇆ KDDGC + H_2O	4.2.1.39	Gluconate dehydratase	Elzainy et al. (1973), Kersters and de Ley (1975), Martinelli and Kinghorn (1994)	ANIG		
r171	:	KDDGC ⇆ PYR + GLYAL	4.1.2.14	2-keto-3-deoxygluconate aldolase	Elzainy et al. (1973), Allam et al. (1975), Martinelli and Kinghorn (1994)	ANIG		
Galactose/Galactitol metabolism								
r172	:	GALOL + NADP ⇆ GLAC + NADPH	1.1.1.21	Aldehyde reductase (Polyol dehydrogenase ($NADP^+$))	Martinelli and Kinghorn (1994)	ANIG, ANID	An01g14880; An16g01720	46249; 53686
r173	:	ATP + GLAC ⇒ ADP + GAL1P	2.7.1.6	Galactokinase	Martinelli and Kinghorn (1994)	ANIG, ANID	An16g04160	56431
r174	:	UTP + GAL1P ⇆ PPI + UDPGAL	2.7.7.10	UTP-hexose-1-phosphate uridylyltransferase (UDP-galactose pyrophosphorylase)	Martinelli and Kinghorn (1994)	ANIG, ANID	An02g03590	174413

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r175	:	UDPGAL ⇆ UDPG	5.1.3.2	UDPglucose 4-epimerase	Martinelli and Kinghorn (1994)	ANIG, ANID	An01g12220; An01g11440; An02g08750; An12g04260; An12g10410; An14g03820	55278; 35645; 175089; 135865; 45989; 56583
r176	:	UTP + G1P ⇒ PPI + UDPG	2.7.7.9	UTP-glucose-1-phosphate uridylyltransferase (UDP glucose pyrophosphorylase)	Martinelli and Kinghorn (1994)	ANIG, ANID	An12g00820	212837
r177	:	G6P ⇆ G1P	5.4.2.2	Phosphoglucomutase	Khanna and Tewari (1963), Martinelli and Kinghorn (1994)	ANIG, ANID	An02g07650	55590
r178	:	UDPG + GAL1P ⇆ G1P + UDPGAL	2.7.7.12	UDP-glucose-hexose-1-phosphate uridylyltransferase		ANID	An02g03590	174413
Galactonic acid/Galactonate metabolism								
r179	:	GLAC + NAD ⇆ GALN14LAC + NADH	1.1.1.48	Galactose 1-dehydrogenase	David et al. (2003)	ANIG, ANID		
r180	:	GALN14LAC + H_2O ⇆ GALNT	3.1.1.25	1,4-Lactonase (gamma-Lactonase)	David et al. (2003)	ANIG	An05g02030; An16g06620	212961; N/A
r181	:	GALNT ⇆ 2D3DGALT + H_2O	4.2.1.6	Galactonate dehydratase	David et al. (2003), Elshafei et al. (1995, A. terreus)	ANIG, ANID	An04g02760	50500
r182	:	2D3DGALT ⇆ PYR + GLYAL	No EC	2-Dehydro-3-deoxy-D-galactonate aldolase	David et al. (2003), Elshafei et al. (1995, A. terreus)	ANIG		
Galacturonate degradation					Witteveen et al. (1990a, Inferred)			
r1215	:	ATP + GALUNT ⇆ GALUNTP + ADP	2.7.1.44	Galacturonokinase		ANEW		
r1216	:	GALUNTP + UTP ⇆ UDPGALU + PPI	No EC	Galacturonate-1-phosphate uridylyl transferase		ANEW		
r1217	:	UDPGALU + 2 NADH ⇆ UDPGAL + 2 NAD + H_2O	1.1.1.-	UDP-D-galactose dehydrogenase		ANEW		
Rhamnose metabolism					de Vries et al. (2002), Fries and Kallstromer (1965)			
r1218	:	RHA ⇆ RHAMN	5.3.1.14	L-Rhamnose isomerase	Fries and Kallstromer (1965, Inferred)	ANEW		
r1219	:	ATP + RHAMN ⇆ ADP + RHAMNP	2.7.1.5	L-Rhamnulose kinase	Fries and Kallstromer (1965, Inferred)	ANEW		
r1220	:	RHAMNP ⇆ T3P2 + LACAL	4.1.2.19	Rhamnulose phosphate aldolase	Fries and Kallstromer (1965, Inferred)	ANEW		
Mannose/Mannitol, Fructose and Sorbose/Sorbitol metabolism								
r184	:	ATP + MAN ⇒ ADP + MAN6P	2.7.1.1	Hexokinase (hxk) (mannokinase)	Martinelli and Kinghorn (1994), Panneman et al. (1998)	ANIG, ANID	An02g14380; An06g00380; An13g00510	55651; 134301; 50817
r185	:	MAN6P ⇆ F6P	5.3.1.8	Mannose-6-phosphate isomerase	Martinelli and Kinghorn (1994)	ANIG, ANID	An08g06350; An04g03200	55763; 44098
r186	:	ATP + FRU ⇒ ADP + F6P	2.7.1.1	Hexokinase (hxk)	Martinelli and Kinghorn (1994), Panneman et al. (1998), Karaffa et al. (2001)	ANIG, ANID	An02g14380; An06g00380; An13g00510	55651; 134301; 50817
r187	:	F6P + NADH ⇆ MNT1P + NAD	1.1.1.17	Mannitol-1-phosphate 5-dehydrogenase	Kiser and Niehaus Jr (1981), Martinelli and Kinghorn (1994)	ANIG, ANID	An02g05830	55560
r188	:	MNT1P + H_2O ⇒ MNT + PI	3.1.3.22	Mannitol-1-phosphatase (Mannitol-1-phosphate phosphatase)	Hult et al. (1980)	ANIG, ANID		
r189	:	MNT + NADP ⇆ FRU + NADPH	1.1.1.138	Mannitol 2-dehydrogenase ($NADP^+$)	Martinelli and Kinghorn (1994)	ANIG, ANID	An06g00750	177668
r190	:	MNT + ATP ⇒ MNT1P + ADP	3.1.3.22	Mannitol kinase	Martinelli and Kinghorn (1994)	ANEW		
r191	:	MAN1P ⇆ MAN6P	5.4.2.8	Phosphomannomutase		ANID	An07g06780; An18g06500	209558; 132771
r192	:	GTP + MAN1P ⇒ PPI + GDPMAN	2.7.7.13	Mannose-1-phosphate guanylyltransferase		ANID	An11g02380; An04g04990	55950; 204833
r193	:	ATP + F6P ⇒ ADP + F26P	2.7.1.105	6-Phosphofructo-2-kinase (Phosphofructokinase 2)	Kubicek-Pranz et al. (1990), Harmsen et al. (1992), Karaffa et al. (2001)	ANIG, ANID	An07g02100; An15g00200	128609; 209963
r194	:	F26P + H_2O ⇒ F6P + PI	3.1.3.46	D-Fructose-2,6-bisphosphate 2-phosphohydrolase		ANID	An07g02100; An15g00200	128609; 209963
r195	:	IDOL + NAD ⇒ SOR + NADH	1.1.1.14	L-Iditol 2-dehydrogenase (NAD-dependent sorbitol dehydrogenase)	Desai et al. (1969c)	ANID	An09g03900; An12g00030; An16g01700; An16g01710	188914; 203198; 183939; 183900
r196	:	SOR + NADH ⇒ SOT + NAD	1.1.99.21	D-Sorbitol dehydrogenase (acceptor)	Desai et al. (1967)	ANIG, ANID	An01g03480; An01g10920; An03g05190; An14g03510	206203; 46405; 50731; 185262
r197	:	SOT + NAD ⇆ FRU + NADH	1.1.1.9	Sorbitol (glucitol) dehydrogenase (NAD+)	Desai et al. (1967, 1969b,c), Witteveen et al. (1994)	ANIG, ANID	An05g02260; An08g09380; An15g04610	212968; 37988; 48775
DISACCHARIDES METABOLISM								

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
Trehalose Biosynthesis								
r198	:	UDPG + G6P ⇒ UDP + TRE6P	2.4.1.15	Alpha,alpha-trehalose-phosphate synthase (UDP-forming) 1 (tpsA, tpsB)	Wolschek and Kubicek (1997), Karaffa et al. (2001)	ANIG, ANID	An07g08710; An08g10510; An14g02180	55704; 211004
Hydrolysis								
r199	:	TRE6P + H_2O ⇒ TRE + PI	3.1.3.12	Trehalose-phosphatase	Arisan-Atac et al. (1996)	ANIG, ANID	An11g10990	119446
r200	:	TRE + H_2O ⇒ 2 DGLC	3.2.1.28	Alpha,alpha-trehalase	David et al. (2003), d'Enfert and Fontaine (1997, A. nidulans)	ANIG, ANID	An01g01540	52061
Maltose								
r201	:	MLT + H_2O ⇒ 2 GLC	3.2.1.20	Alpha-glucosidase (Maltase) (aglA)	Smirnov and Chubova (1965), Rudick et al. (1979), den Herder et al. (1992), Martinelli and Kinghorn (1994)	ANIG, ANID	An13g03710; An01g04880; An07g00350; An09g05880	50927; 55419; 40261; 128654
r202	:	MLTe + H_2Oe ⇒ 2 GLCe	3.2.1.20	Alpha-glucosidase (Maltase) (aglA/aglU)	Smirnov and Chubova (1965), Rudick et al. (1979), den Herder et al. (1992), Martinelli and Kinghorn (1994)	ANIG, ANID	An04g06920	214233
Lactose								
r203	:	LACT + H_2O ⇒ GLC + GLAC	3.2.1.23	β-galactosidase	Martinelli and Kinghorn (1994)	ANID	An01g10350; An06g00290	46429; 177434
r204	:	LACTe + H_2Oe ⇒ GLCe + GLACe	3.2.1.23	β-galactosidase (*lacA*)	Widmer and Leuba (1979), Sykes et al. (1983), Martinelli and Kinghorn (1994), Manzanares et al. (1998), de Vries et al. (1999a)	ANIG, ANID	An01g12150; An07g04420; An14g05820	51764; 180727; 41910
Melibiose								
r205	:	MELIe + H_2Oe ⇒ GLCe + GLACe	3.2.1.22	Alpha-galactosidase (melibiase) (*aglA*, *aglC*)	Manzanares et al. (1998), de Vries and Visser (2001), Wallis et al. (2001)	ANID	An09g00260; An09g00270; An01g01320; An02g11150; An06g00170; An11g06330; An14g01800	212736; 212736; 172232; 207264; 37736; 39180; 185285
Stachyose / Raffinose / Sucrose degradation								
r228	:	STACe + H_2Oe ⇆ RAFFe + GLACe	3.2.1.22	α-galactosidase	Knap et al. (1994), Manzanares et al. (1998), de Vries and Visser (2001)	ANEW	An09g00260; An09g00270; An01g01320; An02g11150; An06g00170; An11g06330; An14g01800	212736; 212736; 172232; 207264; 37736; 39180; 185285
r229	:	RAFFe + H_2Oe ⇆ SUCe + GLACe	3.2.1.22	α-galactosidase	Adya and Elbein (1977), Boddy et al. (1993), Knap et al. (1994), Manzanares et al. (1998), Wallis et al. (2001)	ANEW	An09g00260; An09g00270; An01g01320; An02g11150; An06g00170; An11g06330; An14g01800	212736; 212736; 172232; 207264; 37736; 39180; 185285
r230	:	SUCe + H_2Oe ⇒ FRUe + GLCe	3.2.1.26	Invertase (suc1)	Schreferl-Kunar et al. (1989), Berges et al. (1993), Boddy et al. (1993), Martinelli and Kinghorn (1994), L'Hocine et al. (2000), Yanai et al. (2001)	ANIG	An08g11070; An15g00320	198063; N/A
METABOLISM OF AROMATICS								
Phenylalanine/phenylacetate degradation					Kishore et al. (1976)			
r386	:	PHPYR ⇒ PHAL + CO_2	4.1.1.43	Phenylpyruvate decarboxylase	Kishore et al. (1976)	ANEW		
r387	:	PHAL + NAD + H_2O ⇆ PHAC + NADH	1.2.1.39	Phenylacetaldehyde dehydrogenase	Kishore et al. (1976, Inferred)	ANEW	An02g04110	175251
r388	:	PHAC + O_2 + NADPH ⇒ 2HPAC + H_2O + NADP	No EC	Phenylacetate 2-hydroxylase	Kishore et al. (1976)	ANEW		
r389	:	2HPAC + O_2 + NADPH ⇒ HOMOGEN + H_2O + NADP	No EC	2-Phenylacetate 5-hydroxylase	Kishore et al. (1976, Inferred)	ANEW		
r390	:	HOMOGEN + O_2 ⇆ MACAC	1.13.11.5	Homogentisate oxygenase	Kishore et al. (1976), Sugumaran and Vaidyanathan (1978)	ANID	An11g00430	178499
r391	:	MACAC ⇆ FUACAC	5.2.1.2	Maleylacetoacetate isomerase	Sugumaran et al. (1973)	ANID	An07g06280	180792
r392	:	FUACAC + H_2O ⇒ FUM + ACTAC	3.7.1.2	Fumarylacetoacetase	Sugumaran et al. (1973)	ANID	An02g10000; An04g04150	37286; N/A
r393	:	PHAC + O_2 + NADPH ⇒ 4HPAC + H_2O + NADP	No EC	Phenylacetate hydroxylase	Kishore et al. (1976)	ANEW		
r394	:	4HPAC + NADPH + O_2 ⇆ 4HMAND + H_2O + NADP	No EC	4-hydroxyphenylacetic acid monoxygenase	Kishore et al. (1976, Inferred)	ANEW		
r395	:	4HMAND + NADP ⇒ 4HBFOR + NADPH	No EC	4-hydroxymandelate dehydrogenase	Kishore et al. (1976)	ANEW		
r396	:	4HMAND + NAD ⇒ 4HBFOR + NADH	No EC	4-hydroxymandelate dehydrogenase	Kishore et al. (1976)	ANEW		
r397	:	4HBFOR ⇒ 4HBAL + CO_2	No EC	4-hydroxybenzoylformic acid decarboxylase	Kishore et al. (1976)	ANEW		

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r398	:	4HBAL + NAD + H_2O ⇆ 4HBA + NADH	No EC	4-hydroxybenzaldehyde dehydrogenase	Kishore et al. (1976)	ANEW		
r399	:	4HBA + NADPH + O_2 ⇆ PCC + NADP + H_2O	1.14.13.33	4-hydroxybenzoate 3-hydroxylase	Kishore et al. (1976), Shailubhai et al. (1982), Boschloo et al. (1990), Martinelli and Kinghorn (1994)	ANEW		
Coumarate degradation					Milstein et al. (1988)	ANEW		
r1192	:	COUM + H_2O ⇆ AC + 4HBAL	No EC	Inferred reaction from Milstein et al. (1988)	Milstein et al. (1988, Inferred)	ANEW		
Dimethylterephthalate degradation					Ganji et al. (1995), Kanehisa et al. (2002)			
r1193	:	DMT + H_2O ⇆ MTPHTH + METHOL		Dimethylterephthalate esterase	Ganji et al. (1995)	ANEW		
r1194	:	MTPHTH + H_2O ⇆ TPHTH + METHOL		Dimethylterephthalate esterase	Ganji et al. (1995)	ANEW		
r1195	:	TPHTH + NADPH + O_2 ⇆ DHCHDDC + NADP	1.14.12.15	1,4-dicarboxybenzoate 1,2-dioxygenase	Kanehisa et al. (2002), Ganji et al. (1995, Inferred)	ANEW		
r1196	:	DHCHDDC + NADP ⇆ PCC + CO_2 + NADPH	1.3.1.61	cis-4,5-dihydroxycyclohexa-1(6),2-diene-1,4-dicarboxylate:$NADP^+$ oxidoreductase (decarboxylating)	Kanehisa et al. (2002), Ganji et al. (1995, Inferred)	ANEW		
3-hydroxybenzoate degradation								
r1210	:	3HBA + O_2 + NADPH ⇆ PCC + NADP + H_2O	1.14.13.23	3-hydroxybenzoate 4-hydroxylase	Premkumar et al. (1969), Kumar et al. (1973), Sugumaran et al. (1973), Faber et al. (2001)	ANEW	An02g13270; An01g08690; An01g15110; An04g08410; An08g06250; An09g01850; An09g03500; An12g04510	37516; 172555; 171519; 51444; 175996; 43449; 212597; 42416
Ferulic acid degradation					Milstein et al. (1988, Inferred)			
r1268	:	FER + ATP + COA ⇒ AMP + PPI + FERCOA	6.2.1.12	Ferulate:CoA ligase (AMP-forming)	Milstein et al. (1988, Inferred)	ANEW	An04g04330; An08g06100; An09g01820; An12g02430; An14g05630	44006; 38230; 188806; 43775; 184942
r1269	:	FERCOA + H_2O ⇆ FERHCOA	4.2.1.101	trans-feruloyl-CoA hydratase	Milstein et al. (1988, Inferred)	ANEW		
r1270	:	FERHCOA ⇆ VANIN + ACCOA	4.1.2.41	vanillin synthase	Milstein et al. (1988, Inferred)	ANEW		
r1271	:	VANIN + NAD + H_2O ⇆ VAN + NADH	1.2.1.67	vanillin dehydrogenase	Milstein et al. (1988, Inferred)	ANEW		
Vanillate degradation					Milstein et al. (1988), Lesage-Meessen et al. (1996)			
r1200	:	VAN ⇒ GUA + CO_2	No EC	vanillate decarboxylase	Milstein et al. (1988, Inferred)	ANEW		
r1201	:	GUA + NADPH + O_2 ⇆ CCL + NADP + H_2O + FALD	2.1.1.6	S-adenosyl-L-methionine:catechol O-methyltransferase	Milstein et al. (1988, Inferred)	ANEW	An04g04700; An15g02990; An17g00200	190631; 40535; N/A
Benzonitrile degradation								
r958	:	BN + 2 H_2O ⇆ BA + NH_3	3.5.5.1	benzonitrilase	Snajdrova et al. (2004)	ANEW	An16g00550; An01g07510; An01g12090; An06g01960; An08g08940; An08g10150; An12g01260; An16g06210; An18g01740	41410; 35944; 170270; 175987; N/A; 52578; 141873; 40928; 211815
r959	:	BA + NADPH + O_2 ⇒ 4HBA + NADP + H_2O	1.14.13.12	benzoate 4-monooxygenase (benzoate-para-hydroxylase A, bphA)	Reddy and Vaidyanathan (1975), Boschloo et al. (1990), van Gorcom et al. (1990), Boschloo et al. (1991), Faber et al. (2001), Malonek et al. (2004)	ANEW	An02g13270; An01g08690; An01g15110; An04g08410; An08g06250; An09g01850; An09g03500; An12g04510	37516; 172555; 171519; 51444; 175996; 43449; 212597; 42416
Indole degradations					Subba Rao et al. (1971), Kamath and Vaidyanathan (1990)			
r1206	:	IND + O_2 + NADPH ⇆ 3HIND + H_2O + NADP	No EC	indole monooxygenase	Kamath and Vaidyanathan (1990)	ANEW		
r1207	:	3HIND + O_2 ⇆ NFAN	No EC	3-hydroxyindoxyl dioxygenase	Kamath and Vaidyanathan (1990)	ANEW		
r1208	:	NFAN + H_2O ⇆ FOR + AN	3.5.1.9	N-formylanthranilate deformylase	Kamath and Vaidyanathan (1990)	ANEW		
Tannic acid degradation					Ramirez-Coronel et al. (2003), Bhardwaj et al. (2003), van Diepeningen et al. (2004)			

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r1222	:	TANAe + 10 $H_2Oe \Rightarrow$ 10 345THBe + GLCe	3.1.1.20	tannin acyl hydrolase (tannase)	Ramirez-Coronel et al. (2003), Bhardwaj et al. (2003), van Diepeningen et al. (2004)	ANEW	An01g02740; An01g11560; An01g14800; An02g00350; An03g05300; An04g04430; An08g08140; An08g09800; An09g00890; An10g00910; An10g00950; An11g01220; An11g03590; An12g10390; An13g03810; An17g00830	N/A; 35636; 35388; 172914; 44518; 191085; N/A; 175881; 189231; 50972; 50973; 178324; 38960; 51478; 131509; 45118
Tryptophan degradation								
r400	:	TRP + $O_2 \Rightarrow$ FKYN	1.13.11.11	Indoleamine 2,3-dioxygenases, Tryptophan 2,3-dioxygenase	Subba Rao et al. (1971)	ANID	An04g07210	45277
r401	:	FKYN + $H_2O \Rightarrow$ FOR + KYN	3.5.1.49	Kynurenine formamidase (formamidase)	Subba Rao et al. (1971)	ANID	An07g05830	180458
r402	:	KYN + $H_2O \Rightarrow$ ALA + AN	3.7.1.3	Kynureninase	Subba Rao et al. (1971), Shetty and Gaertner (1975)	ANID	An04g07200; An16g04630	45278; 210508
r403	:	AN + NADPH + $O_2 \leftrightarrows$ DHBA + NADP + NH_3	1.14.13.35	anthranilate 3-monooxygenase (deaminating)	Sreeleela et al. (1969), Subba Rao et al. (1971), Subramanian and Vaidyanathan (1984), Kamath and Vaidyanathan (1990)	ANEW		
r404	:	DHBA $\Rightarrow$ CCL + CO_2	4.1.1.46	2,3-Dihydroxybenzoate carboxylyase (dhbD)	Rao et al. (1967), Subba Rao et al. (1971), Ramachandran et al. (1979), Kamath et al. (1987), Kamath and Vaidyanathan (1990), Santha et al. (1995)	ANEW	An07g02050; An02g05560	209864; 36964
3-Hydroxykynurenine degradation								
r406	:	HKYN + $H_2O \Rightarrow$ HAN + ALA	3.7.1.3	Kynureninase	Shetty and Gaertner (1975)	ANEW	An04g07200; An16g04630	45278; 210508
Tyrosine degradation								
r411	:	4HPP + $O_2 \Rightarrow$ HOMOGEN + CO_2	1.13.11.27	4-hydroxyphenylpyruvate dioxygenase	Utkin (1950)	ANEW	An04g01280; An07g01900	190603; 124205
Salicylic acid degradation					Krupka et al. (1967), Shailubhai et al. (1982, 1983)	ANEW		
r968	:	SALI + NADPH + $O_2 \leftrightarrows$ CCL + NADP + H_2O + CO_2	1.14.13.1	Salicylate hydroxylase	Krupka et al. (1967), Shailubhai et al. (1982, 1983)	ANEW	An01g07130; An02g01050; An03g00530; An03g01540; An03g02130; An03g05310; An03g06690; An04g07370; An05g01200; An07g00550; An07g05650; An07g06800; An09g00590; An09g01840; An09g04390; An11g02480; An11g03060; An11g03150; An11g05130	172298; 36659; 45799; 133101; 194221; 191298; 191475; 45265; N/A; 181136; 46219; N/A; 50241; 188800; 189090; 178872; 178362; 38917; 208837
Benzoylamine degradation								
r979	:	BAMN + H_2O + $O_2 \leftrightarrows$ BAL + H_2O_2 + NH_3	1.4.3.6	Amine oxidase (AO-I and AO-II)	Schilling and Lerch (1995a), Frebort et al. (1999)	ANEW	An02g10920; An09g01550; An03g00730; An07g06400; An12g03290; An13g00710; An17g00010	37354; 54408; 45789; 120706; 57198; 204355
Mandelate degradation					Jamaluddin et al. (1970)	ANEW		
r974	:	DMAND + NAD $\leftrightarrows$ NADH + BFOR	DMAN	D-mandelate dehydrogenase	Jamaluddin et al. (1970), Ramanarayanan and Vaidyanathan (1973)	ANEW	An03g05150	50728

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r975	:	LMAND + NAD ⇆ NADH + BFOR	LMAN	L-mandelate dehydrogenase	Jamaluddin et al. (1970)	ANEW		
r976	:	BFOR ⇒ CO_2 + BAL	4.1.1.7	benzoylformate decarboxylase	Jamaluddin et al. (1970)	ANEW	An02g05590	52239
r977	:	BAL + NAD + H_2O ⇒ BA + NADH	1.2.1.6	NAD-benzaldehyde dehydrogenase	Raman and Shanmugasundaram (1962), Jamaluddin et al. (1970)	ANEW		
r978	:	BAL + NADP + H_2O ⇒ BA + NADPH	1.2.1.7	NADP-benzaldehyde dehydrogenase	Jamaluddin et al. (1970), Kishore et al. (1976)	ANEW		
Resorcinol degradation					Shailubhai et al. (1982, 1983)	ANEW		
r971	:	RES + O_2 + NADPH ⇆ BTOL + NADP + H_2O	1.3.1.32	Resorcinol hydroxylase	Shailubhai et al. (1982, 1983)	ANEW		
r972	:	BTOL + O_2 ⇆ 2MAC	1.13.11.37	hydroxyquinol 1,2-dioxygenase	Shailubhai et al. (1982, 1983)	ANEW	An01g12310	46358
Hydroxyquinol pathway								
r973	:	2MAC + NADPH ⇆ 3OA + NADP	1.3.1.32	maleylacetate reductase	Shailubhai et al. (1982, 1983)	ANEW	An03g05490; An07g09360	44532; 48257
Gentisate pathway					Kanehisa et al. (2002), Yogambal and Karegoudar (1997, Inferred)			
r980	:	HOMOGEN + O_2 ⇒ GNTAL + CO_2 + H_2O	1.13.12.-	Homogentisate monooxidase		ANEW		
r981	:	GNTAL + H_2O + O_2 ⇒ GEN + H_2O_2	1.2.3.1			ANEW		
r982	:	GEN + O_2 ⇆ 3MPYR	1.13.11.4	gentisate 1,2-dioxygenase	Yogambal and Karegoudar (1997), Kishore et al. (1976, Inferred)	ANEW	An02g12800; An11g10310; An18g01020	135462; 125331; 187293
r983	:	3MPYR ⇆ 3FPYR	5.2.1.4	maleylpyruvate isomerase	Yogambal and Karegoudar (1997), Kishore et al. (1976, Inferred)	ANEW		
r984	:	3FPYR + H_2O ⇆ FUM + PYR	3.7.1.5	acylpyruvate hydrolase	Yogambal and Karegoudar (1997), Kishore et al. (1976, Inferred)	ANEW		
Catechol and protocatechuate pathways					Cook and Cain (1977), Martinelli and Kinghorn (1994), Mazur et al. (1994), Kuswandi and Roberts (1992, A. nidulans)	ANEW		
r960	:	CCL + O_2 ⇆ MUCO	1.13.11.1	catechol 1,2-dioxygenase	Shailubhai et al. (1983), Sahasrabudhe et al. (1986), Milstein et al. (1988), Kamath and Vaidyanathan (1990)	ANEW		
r961	:	MUCO ⇆ MUCL	5.5.1.1	muconate cycloisomerase	Thatcher and Cain (1972)	ANEW	An01g14730	205361
r962	:	MUCL ⇆ OAEL	5.3.3.4	muconolactone delta-isomerase	Halsall et al. (1969)	ANEW		
r963	:	DHSK ⇆ PCC + H_2O	4.2.1.10	5-dehydroshikimate dehydrase	Cain (1972b)	ANEW	An08g06800	207929
r964	:	PCC + O_2 ⇆ 3CMUCO	1.13.11.3	protocatechuate 3,4-dioxygenase	Milstein et al. (1988), Martinelli and Kinghorn (1994)	ANEW		
r965	:	3CMUCO ⇆ 4CMUCL	5.5.1.2	3-Carboxy-cis,cis-muconate cycloisomerase	Halsall et al. (1969), Thatcher and Cain (1972), Cook and Cain (1977), Mazur et al. (1994)	ANEW	An14g01340	185353
r966	:	4CMUCL ⇒ OAEL + CO_2	4.1.1.44	4-carboxymuconolactone decarboxylase	Thatcher and Cain (1972)	ANEW	An03g06020	191430
r967	:	OAEL + H_2O ⇆ 3OA	3.1.1.24	3-oxoadipate enol-lactonase	Halsall et al. (1969)	ANEW	An13g01940; An07g07290	44810; 180211
r969	:	3OAm + SUCCOAm ⇆ SUCCm + 3OACOAm	2.8.3.6	3-oxoadipate CoA-transferase	Halsall et al. (1969)	ANEW	An01g00200; An06g01370	172302; 55680
r970	:	3OACOAm + COAm ⇆ ACCOAm + SUCCOAm	2.3.1.16	3-ketoacyl-CoA thiolase	Halsall et al. (1969)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
METABOLISM OF AMINES								
Butylamine								
r1188	:	BUTN + H_2O + O_2 ⇆ BUTAL + H_2O_2 + NH_3	1.4.3.6	Amine oxidase (maoN, AO-I, AO-II)	Frebort et al. (1996), Schilling and Lerch (1995a)	ANEW	An02g10920; An09g01550; An03g00730; An07g06400; An12g03290; An13g00710; An17g00010	37354; 54408; 45789; 120706; 57198; 204355
r1189	:	BUTAL + COA + NAD ⇆ C40COA + NADH	1.2.1.57	Butanal dehydrogenase	Frebort et al. (1996, Inferred)	ANEW		
Pentylamine								
r1202	:	PENN + H_2O + O_2 ⇆ PENAL + H_2O_2 + NH_3	1.4.3.6	Amine oxidase (maoN, AO-I, AO-II)	Frebort et al. (1996), Schilling and Lerch (1995a)	ANEW	An02g10920; An09g01550; An03g00730; An07g06400; An12g03290; An13g00710; An17g00010	37354; 54408; 45789; 120706; 57198; 204355
r1203	:	PENAL + COA + NAD ⇆ C50COA + NADH	1.2.1.57	Butanal dehydrogenase	Schilling and Lerch (1995a, Inferred)	ANEW		
POLYSACCHARIDES METABOLISM								
CELL WALL COMPONENTS								

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
Glucan Biosynthesis								
r206	:	UDPG ⇒ UDP + 13GLUCAN	2.4.1.34	1,3-beta-Glucan synthase	David et al. (2003)	ANIG, ANID	An17g02120	54934
r207	:	UDPG ⇒ UDP + 14GLUCAN	2.4.1.18	1,4-alpha-Glucan branching enzyme	Stagg and Feather (1973)	ANEW	An14g04190	211162
r208	:	UDPG ⇒ UDP + PSNIG	2.4.1.-	1,3-alpha-Glucan (Pseudonigeran) synthase	Horisberger et al. (1972), Damveld et al. (2005)	ANEW	An01g06120; An02g03260; An04g09890; An09g03070; An12g02450; An14g04190; An15g07810	46621; 36809; 55204; 54378; 212915; 211162; 40878
r209	:	UDPG ⇒ UDP + NIG	2.4.1.-	1,3-alpha-1,4-alpha-Glucan (Nigeran) synthase	Bobbitt et al. (1977, Inferred)	ANEW	An01g06120; An02g03260; An04g09890; An09g03070; An12g02450; An14g04190; An15g07810	46621; 36809; 55204; 54378; 212915; 211162; 40878
Chitin Biosynthesis								
r210	:	GLN + F6P ⇒ GLU + GA6P	2.6.1.16	Glutamine-fructose-6-phosphate transaminase (isomerizing)	Ram et al. (2004)	ANIG, ANID	An03g05940; An18g06820	139271; N/A
r211	:	ACCOA + GA6P ⇆ COA + NAGA6P	2.3.1.4	Glucosamine-phosphate N-acetyltransferase	David et al. (2003)	ANIG, ANID	An12g07840	49553
r212	:	NAGA6P ⇆ NAGA1P	5.4.2.3	Phosphoacetylglucosamine mutase	David et al. (2003)	ANIG, ANID	An18g05160; An18g05170	212120; 212120
r213	:	UTP + NAGA1P ⇆ PPI + UDPNAG	2.7.7.23	UDP-N-acetylglucosamine pyrophosphorylase	David et al. (2003)	ANIG, ANID	An12g00480	54451
r214	:	UDPNAG ⇒ UDP + CHIT	2.4.1.16	Chitin synthase (chs1, chs2)	Gomez et al. (1977)	ANIG, ANID	An03g06360; An07g05570; An08g05290; An09g02290; An09g04010; An12g10380; An14g00660	44589; 53259; 38285; 50188; 56923; 45992; 49223
Hydrolysis								
r215	:	CHIT + H_2O ⇒ NAG	3.2.1.14	Chitinase (Endochitinase)	Gomez et al. (1977), Fukazawa et al. (2004)	ANID	An01g05360; An02g07020; An14g07420; An01g05160; An02g13580; An04g04670; An08g09030; An09g06400; An11g01160; An12g02920; An12g05330; An15g00840; An19g00100	170148; 197446; N/A; 196559; 129219; 190616; 38015; 119587; 127214; 189361; N/A; 40367; 122923
r216	:	CHIT + H_2O ⇒ NAG	3.2.1.52	N-Acetyl-beta-glucosaminidase	Gomez et al. (1977), Pera et al. (1997), Jones and Kosman (1980)	ANID	An01g01920; An09g02240	36363; 121359 and 54398
r217	:	NAG + H_2O ⇒ GLCN + AC	3.5.1.33	N-acetylglucosamine deacetylase		ANID	An11g00920; An18g04560	199058; 126860
r218	:	ATP + GLCN ⇒ ADP + GA6P	2.7.1.1	Hexokinase (hxk)	Panneman et al. (1998)	ANID	An02g14380; An06g00380; An13g00510	55651; 134301; 50817
r219	:	CHIT + H_2O ⇒ CHITO + AC	3.5.1.41	Chitin deacetylase		ANID	An04g07110; An02g13530; An12g04480	45285; 173767; 186040
Galactosaminogalactan								
r220	:	UDPNAG ⇆ UDPNAGAL	5.1.3.7	UDP-N-acetylglucosamine 4-epimerase	Bardalaye and Nordin (1976, Inferred)	ANEW		
r221	:	0.754 UDPGAL + 0.181 UDPNAGAL + 0.065 UDPG ⇒ GAG + UDP	No EC	Lumped reaction for biosynthesis of galactosaminogalactan	Bardalaye and Nordin (1976, Inferred)	ANEW		
Galactoglucomannan								
r222	:	0.435 UDPGAL + 0.435 GDPMAN + 0.13 UDPG ⇒ GGM + 0.565 UDP + 0.435 GDP	No EC	Lumped reaction for biosynthesis of galactoglucomannan	Bardalaye and Nordin (1977, Inferred)	ANEW		

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
ENERGY METABOLISM									
r235	:	NADHm + Qm ⇒ QH_2m + NADm	1.6.5.3	NADH-ubiquinone oxidoreductase (nad5, nuo51, nd4L)	Promper et al. (1993), Juhász et al. (2004)	ANIG, ANID	*	An02g05470; An02g05880; An02g09730; An02g11200; An04g00060; An04g00110; An04g05640; An06g01390; An07g04180; An08g04240; An08g04910; An08g10690; An09g06850; An11g06200; An11g08840; An11g09350; An11g09390; An12g04780; An12g07520; An14g00060	206795; 55562; 174046; 207272; 54674; 213396; 55011; 37834; 209689; 208150; 52695; 207707; 56863; 208884; 143222; 208985; 199481; 56704; 201966; 201294
r236	:	PPI + H_2O ⇒ 2 PI	3.6.1.1	Inorganic diphosphatase	Pathak and Sreenivasan (1955), Rama and Shanmugasundaram (1985)	ANIG, ANID		An02g12010	207331
r237	:	PPIm + H_2O ⇒ 2 PIm	3.6.1.1	Inorganic diphosphatase	David et al. (2003)	ANIG, ANID		An02g12010	207331
r238	:	QH_2m + 0.5 O_2m ⇒ Qm + H_2Om	UBIOX	Ubiquinol oxidase (mitochondrial alternative oxidase (*aox*))	Kirimura et al. (1999, 2006)	ANIG		An11g04810	47967
r239	:	NADHm + Qm + 4 H^+_POm ⇒ NADm + QH_2m + 4 H^+_PO	1.6.5.3	Respiratory-chain NADH dehydrogenase (*nad5*, *nuo51*, *nd4L*)	Promper et al. (1993), Juhász et al. (2004)	ANIG, ANID	*	An02g05470; An02g05880; An02g09730; An02g11200; An04g00060; An04g00110; An04g05640; An06g01390; An07g04180; An08g04240; An08g04910; An08g10690; An09g06850; An11g06200; An11g08840; An11g09350; An11g09390; An12g04780; An12g07520; An14g00060	206795; 55562; 174046; 207272; 54674; 213396; 55011; 37834; 209689; 208150; 52695; 207707; 56863; 208884; 143222; 208985; 199481; 56704; 201966; 201294
r240	:	NADH + Qm + 4 H^+_POm ⇒ NAD + QH_2m + 4 H^+_PO	1.6.5.3	Proton pumping Mitochondrial NADH dehydrogenase that catalyzes the oxidation of cytosolic NADH	Promper et al. (1993)	ANEW	*	An02g05470; An02g05880; An02g09730; An02g11200; An04g00060; An04g00110; An04g05640; An06g01390; An07g04180; An08g04240; An08g04910; An08g10690; An09g06850; An11g06200; An11g08840; An11g09350; An11g09390; An12g04780; An12g07520; An14g00060	206795; 55562; 174046; 207272; 54674; 213396; 55011; 37834; 209689; 208150; 52695; 207707; 56863; 208884; 143222; 208985; 199481; 56704; 201966; 201294

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r241	:	NADH + Qm ⇒ QH_2m + NAD	1.6.5.3	NADH-ubiquinone oxidoreductase (nad5, nuo51, nd4L)	Promper et al. (1993), Juhász et al. (2004)	ANIG, ANID	*	An02g05470; An02g05880; An02g09730; An02g11200; An04g00060; An04g00110; An04g05640; An06g01390; An07g04180; An08g04240; An08g04910; An08g10690; An09g06850; An11g06200; An11g08840; An11g09350; An11g09390; An12g04780; An12g07520; An14g00060	206795; 55562; 174046; 207272; 54674; 213396; 55011; 37834; 209689; 208150; 52695; 207707; 56863; 208884; 143222; 208985; 199481; 56704; 201966; 201294
r242	:	NADPH + 2 FERIm ⇒ NADP + 2 FEROm	1.6.2.4	NADPH-ferrihemoprotein reductase (cprA)	van den Brink et al. (1996)	ANID		An04g06960; An05g00510; An08g07840	54972; 49744; 198350
r243	:	QH_2m + 2 FERIm + 4 H^+_POm ⇒ Qm + 2 FEROm + 4 H^+_PO	1.10.2.2	Ubiquinol-cytochrome c reductase	David et al. (2003)	ANIG, ANID	*	An01g12210; An01g06180; An04g05220; An08g06550; An14g04080	205553; 205959; 57369; 177548; 211145
r244	:	2 FEROm + 0.5 O_2m + 4 H^+_POm ⇒ 2 FERIm + H_2Om + 4 H^+ H^+ H^+_PO	1.9.3.1	Cytochrome c oxidase subunit I (*cox5*)	Kirimura et al. (2000), Juhász et al. (2004)	ANIG, ANID	*	An02g01720; An02g09930; An04g01560; An07g07390; An08g01550; An09g03990; An11g10200; An14g04170	206489; 207204; 213247; 199998; 175806; N/A; 209100; 211156
r245	:	ADPm + PIm + 3.88 H^+_PO ⇒ ATPm + H_2Om + 3.88 H^+_POm	3.6.3.14	F1F0-ATPase complex	David et al. (2003), Blair et al. (1996, A. nidulans)	ANIG, ANID	*	An01g04630; An01g04930; An01g10880; An02g04520; An02g06240; An07g06560; An12g00640; An12g04950; An14g04180; An16g07290; An16g07410	36164; 206061; 196131; 206734; N/A; N/A; 138230; 128507; 211159; 214565; 204982
r246	:	ATPm + H_2Om + 3.88 H^+_POm ⇒ ADPm + PIm + 3.88 H^+_PO	3.6.3.6	Mitochondrial membrane ATPase 1	Jernejc and Legisa (2001)	ANID		An12g08760	201858
r257	:	ATP + H_2O + 3.88 H^+ ⇒ ADP + PI + 3.88 H^+e	3.6.3.6	Plasma membrane ATPase 1		ANEW		An01g05670	171582
r247	:	ATP + H_2O + H^+ + Ke ⇒ ADP + PI + H^+e + K	3.6.3.10	Potassium-transporting ATPase		ANID		An02g06350; An02g09470; An02g09480; An08g03090; An12g04500; An17g02310; An19g00350	55567; 207175; 207175; 38450; 54015; 214148; 138839
r248	:	ATP + H_2O + H^+ + Cae ⇒ ADP + PI + H^+e + Ca	3.6.3.8	Calcium-transporting ATPase		ANID		An02g06350; An02g09470; An02g09480; An08g03090; An12g04500; An17g02310; An19g00350	55567; 207175; 207175; 38450; 54015; 214148; 138839

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r249	:	2 FERIm + LLACm ⇒ PYRm + 2 FEROm	1.1.2.3	Lactic acid dehydrogenase		ANID	An04g02840; An04g08560; An11g03500; An12g06530; An14g02250	213113; 45912; 140694; 186062; 211015
r250	:	2 FERIm + LACm ⇒ PYRm + 2 FEROm	1.1.2.4	Mitochondrial enzyme D-lactate ferri-cytochrome c oxidoreductase		ANID	An02g10670; An12g06290	47113; 186792
r251	:	ADP + PI + ATPm + H_2Om + H^+_PO ⇒ ADPm + PIm + ATP + H_2O + H^+_POm	MCF	ADP/ATP translocase	David et al. (2003)	ANIG, ANID	An18g04220	212044
r252	:	NADPH + O_2 ⇒ NADP + H_2O_2	1.6.3.1	NADPH oxidase		ANID	An08g10000	52585
r253	:	NADPH + Qm ⇒ QH_2m + NADP	1.6.99.1	NADPH dehydrogenase (quinone) (NADPH oxidase)	David et al. (2003)	ANIG, ANID	An11g08510	39329
r254	:	FADH2m + Qm ⇒ FADm + QH_2m	1.5.5.1	Electron-transferring-flavoprotein dehydrogenase		ANID	An16g03910	210584
Oxygen metabolism								
r255	:	2 H_2O_2 ⇒ 2 H_2O + O_2	1.11.1.6	Catalase (catR)	Horie et al. (1976), Gruft et al. (1978), Kikuchi-Torii et al. (1982), Witteveen et al. (1992), Fowler et al. (1993), Fiedurek (2000), Martinelli and Kinghorn (1994)	ANIG, ANID	An01g01820; An03g05660; An01g01550	206342; 213578; 55494
r256	:	2 H_2O_2e ⇒ 2 H_2Oe + O_2e	1.11.1.6	Catalase (catR)	Martinelli and Kinghorn (1994), Witteveen et al. (1992), Rogalski et al. (1998)	ANIG, ANID	An03g05660; An01g01550	213578; 55494
AMINO ACID METABOLISM								
Alanine, aspartate and asparagine biosynthesis					Kanehisa et al. (2002)			
r258	:	OA + GLU ⇆ ASP + AKG	2.6.1.1	Aspartate transaminase	Patil and Ramakrishnan (1966), Alvarez-Vasquez et al. (2000)	ANID	An03g00050; An03g01120; An04g05130; An09g02390; An12g07870; An16g05570	141281; 45764; 214397; 50187; 186098; 56390
r263	:	ASP + ATP + GLN + H_2O ⇒ GLU + ASN + AMP + PPI	6.3.5.4	Asparagine synthase		ANID	An01g07910; An04g01340; An12g07660	131513; 57091; 186429
r259	:	PYR + GLU ⇆ AKG + ALA	2.6.1.2	Alanine transaminase	Patil and Ramakrishnan (1966)	ANID	An11g02620	208695
r261	:	PYR + NH_3 + NADPH ⇒ ALA + H_2O + NADP	1.4.1.1	Alanine dehydrogenase (NADPH)	Hoshino et al. (1962), Savov et al. (1986)	ANEW		
r262	:	PYR + NH_3 + NADH ⇒ ALA + H_2O + NAD	1.4.1.1	Alanine dehydrogenase (NADH)	Savov et al. (1986)	ANEW		
r259m	:	PYRm + GLUm ⇆ AKGm + ALAm	2.6.1.2	Alanine transaminase	Alvarez-Vasquez et al. (2000)	ANID	An11g02620	208695
r258m	:	OAm + GLUm ⇆ ASPm + AKGm	2.6.1.1	Aspartate transaminase	Patil and Ramakrishnan (1966), Alvarez-Vasquez et al. (2000)	ANID	An04g06380	214270
Aspartate degradation								
r265	:	ASP + H_2O + O_2 ⇒ OA + NH_3 + H_2O_2	1.4.3.2	L-amino acid oxidase	Oganesyan et al. (1998)	ANEW	An08g10800	176790
Asparagine degradation								
r266	:	ASN + H_2O ⇒ ASP + NH_3	3.5.1.1	Asparaginase	Wriston, Jr and Yelling (1973)	ANID	An01g14960; An18g03190	51685; 187609
Arginine metabolism					Kanehisa et al. (2002)			
r267	:	ORN + AKG ⇒ GLUGSAL + GLU	2.6.1.13	Ornithine transaminase		ANEW	An04g04130; An11g08870	54525; 48081
r271	:	SAM ⇆ DSAM + CO_2	4.1.1.50	S-adenosylmethionine decarboxylase		ANID	An09g06050	54311
r274	:	GBAD ⇒ GBAT + NH_3	3.5.1.4	Amidase/acetamidase		ANID	An16g07500; An01g12500; An02g00190; An02g00340; An03g05880; An07g00100; An07g03960; An09g01020; An09g04990; An11g02980; An11g08900; An12g01020; An14g00670; An15g00290	194059; 35556; 36604; 121987; 191243; 181662; 40014; 121710; 188491; 38912; 48084; 54468; 210891; 181881
r275	:	ARG + H_2O ⇒ ORN + UREA	3.5.3.1	Arginase (argA)	Kiesel (1922), Sukhenko and Podgainaya (1959)	ANID	An02g07250	55582
Urea cycle								
r268m	:	CITRm + ASPm + ATPm ⇆ AMPm + PPIm + ARGSUCCm	6.3.4.5	Argininosuccinate synthase		ANID	An12g01280; An15g02340	43683; 40489
r269m	:	ARGSUCCm ⇆ FUMm + ARGm	4.3.2.1	Argininosuccinate lyase		ANID	An01g06560	51912
r275m	:	ARGm + H_2Om ⇒ ORNm + UREAm	3.5.3.1	Arginase	Kiesel (1922), Sukhenko and Podgainaya (1959)	ANID	An14g01190	41557

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r282m	:	ORNm + CAPm ⇒ CITRm + PIm	2.1.3.3	Ornithine carbamoyltransferase (argB)	Buxton et al. (1987), Swart et al. (1992), Lenouvel et al. (2002)	ANID	An14g03400	N/A
Ornithine cycle								
r277	:	GLUm + ACCOAm ⇒ COAm + NAGLUm	2.3.1.1	Amino-acid N-acetyltransferase		ANID	An03g02930	194534
r278	:	NAGLUm + ATPm ⇒ ADPm + NAGLUPm	2.7.2.8	Acetylglutamate kinase		ANID	An03g01910	194591
r279	:	NAGLUPm + NADPHm ⇒ NADPm + PIm + NAGLUSm	1.2.1.38	N-Acetyl-gamma-glutamyl-phosphate reductase (EC 1.2.1.38) and acetyl-glutamate kinase (EC 2.7.2.8)		ANID	An12g07580	211485
r280	:	NAGLUSm + GLUm ⇒ AKGm + NAORNm	2.6.1.11	Acetylornithine aminotransferase		ANID	An15g02360	35307
r281	:	NAORNm + GLUm ⇒ ORNm + NAGLUm	2.3.1.35	Glutamate N-acetyltransferase		ANID	An03g04330	50689
Cysteine biosynthesis								
r283	:	SER + ACCOA ⇒ COA + ASER	2.3.1.30	Serine transacetylase/serine O-acetyltransferase	Stepien et al. (1975), Sieńko and Paszewski (1999, A. nidulans)	ANID	An09g02800	212646 and 54391
r284	:	ASER + H2S ⇒ AC + CYS	2.5.1.47	Cysteine synthase (cysB) (O-acetylserine sulfhydrylase)	Pieniazek et al. (1973), Stepien et al. (1975), Topczewski et al. (1997, A. nidulans)	ANID	An02g10750; An12g09880; An14g00960; An15g05170; An16g07520	207249; N/A; 184767; 181861; 193596
Cysteine degradation								
r285	:	2 CYS + O_2 ⇒ CYST + H_2O_2	1.8.3.3	Sulfhydryl oxidase (Sox)	Vignaud et al. (2002)	ANEW	An09g05940; An16g02470	189206; 183599
r286	:	2 CYS + NAD ⇒ CYST + NADH	1.8.1.6	Cystine reductase	Kasatkina and Zheltova (1963)	ANEW		
Glutamate and glutamine metabolism								
r289	:	GLU + H_2O + NAD ⇒ AKG + NH_3 + NADH	1.4.1.2	Glutamate dehydrogenase	Patil and Ramakrishnan (1966), Punekar et al. (1985), Savov et al. (1986)	ANID	An02g14590	37620
r290	:	AKG + NH_3 + NADPH ⇒ GLU + H_2O + NADP	1.4.1.4	Glutamate dehydrogenase (gdhA)	Punekar et al. (1985), Savov et al. (1986), Noor and Punekar (2005)	ANID	An04g00990	203758
r291	:	GLU + NH_3 + ATP ⇒ GLN + ADP + PI	6.3.1.2	Glutamate-ammonia ligase	Kim (1981), Punekar et al. (1985), Savov et al. (1986)	ANID	An14g01460; An15g01850	49256; 48679
r292	:	GLN ⇒ GLU + NH_3	3.5.1.2	Glutaminase A	Shi et al. (1996)	ANID	An02g06720; An11g07960	197415; 208953
r287	:	AKG + GLN + NADPH ⇒ NADP + 2 GLU	1.4.1.14	Glutamate synthase (NADPH)	Savov et al. (1986)	ANEW	An01g08800	196278
r288	:	AKG + GLN + NADH ⇒ NAD + 2 GLU	1.4.1.13	Glutamate synthase (NADH)	Savov et al. (1986)	ANEW	An07g09920	209263
r293	:	GLUGSALm + NADPm + 2 H_2Om ⇒ NADPHm + GLUm	1.5.1.12	Delta-1-pyrroline-5-carboxylate dehydrogenase		ANID	An02g02290; An11g06140	52149; 208879
r294	:	P5Cm + NADm + 2 H_2Om ⇒ NADHm + GLUm	1.5.1.12	Delta-1-pyrroline-5-carboxylate dehydrogenase		ANID	An02g02290; An11g06140	52149; 208879
Serine, glycine and threonine biosynthesis								
r295	:	3PG + NAD ⇒ NADH + PHP	1.1.1.95	Phosphoglycerate dehydrogenase	Pei et al. (2003, A. nidulans)	ANID	An11g01390; An12g01580; An17g02330	38797; 128882; 57311
r296	:	PHP + GLU ⇒ AKG + 3PSER	2.6.1.52	Phosphoserine transaminase		ANID	An02g00890	206447
r297	:	3PSER + H_2O ⇒ PI + SER	3.1.3.3	Phosphoserine phosphatase		ANID	An11g09770	179814
r298	:	THF + SER ⇆ GLY + METTHF + H_2O	2.1.2.1	Glycine hydroxymethyltransferase/serine hydroxymethyltransferase	Lewandowska et al. (1996, A. nidulans)	ANID	An05g00410; An16g02970	211700; 56462
r301	:	GLY + ACAL ⇒ THR	4.1.2.5	Threonine aldolase		ANID	An15g03260; An03g01360; An03g02300; An07g00680	40551; 194373; 45688; 56260
r311	:	THR + NAD + H_2O ⇒ GLY + AC + NADH	1.1.1.103	Threonine dehydrogenase		ANID	An05g02000	189384
r306	:	HSER + ATP ⇒ ADP + PHSER	2.7.1.39	Homoserine kinase		ANID	An17g02090	214104
r307	:	PHSER + H_2O ⇒ PI + THR	4.2.3.1	Threonine synthase		ANID	An16g02520	183233
r299	:	GLY + THF + NAD ⇒ METTHF + NADH + CO_2 + NH_3	2.1.2.10	Aminomethyltransferase (2.1.2.10, 1.4.4.2 and 1.8.1.4 lumped)		ANID	An14g01150; An08g03070	210951; 122951
Homoserine biosynthesis								
r302	:	ASP + ATP ⇒ ADP + BASP	2.7.2.4	Aspartate kinase		ANID	An17g02280	54942
r303	:	BASP + NADPH ⇒ NADP + PI + ASPSA	1.2.1.11	Aspartic β semi-aldehyde dehydrogenase, aspartate semialdehyde dehydrogenase		ANID	An11g09510	209010
r304	:	ASPSA + NADH ⇒ NAD + HSER	1.1.1.3	Homoserine dehydrogenase I		ANID	An02g07430	52305
r300	:	ALA + GLX ⇆ PYR + GLY	2.6.1.44	Alanine-glyoxylate transaminase	Oganesyan et al. (2004)	ANID	An09g03830	50140
r308a	:	GLYm + HPLYSm ⇆ HPSAMLYSm + CO_2m	2.1.2.10	Aminomethyltransferase (2.1.2.10, 1.4.4.2 and 1.8.1.4 lumped)		ANEW	An14g01150; An08g03070	210951; 122951
r308b	:	HPSAMLYSm + THFm ⇆ NH_3m + METTHFm + DHPLYSm	2.1.2.1	Glycine hydroxymethyltransferase/serine hydroxymethyltransferase		ANEW	An05g00410; An16g02970	211700; 56462

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r308c	:	DHPLYSm + NADm ⇆ HPLYSm + NADHm	1.4.4.2	Glycine dehydrogenase (decarboxylating) / glycine decarboxylase complex (P-subunit), glycine synthase (P-subunit), glycine cleavage system (P-subunit)		ANEW	An14g01150	210951
Threonine and serine degradation								
r312	:	SER ⇒ PYR + NH_3	4.3.1.17	L-Serine ammonia-lyase		ANID	An04g02220	213166
r313	:	THR ⇒ NH_3 + OBUT	4.3.1.19	Threonine dehydratase	MacDonald et al. (1974, A. nidulans)	ANID	An04g02580	190860
r313m	:	THRm ⇒ NH_3m + OBUTm	4.3.1.19	Threonine dehydratase		ANID	An04g02580	190860
Histidine biosynthesis								
r316	:	R5P + ATP ⇆ PRPP + AMP	2.7.6.1	Ribose-phosphate pyrophosphokinase	Foley et al. (1965), Nielsen et al. (2004, A. nidulans)	ANID	An02g09240; An04g05860; An07g02210	52363; 204746; 209842
r317	:	PRPP + ATP ⇒ PPI + PRBATP	2.4.2.17	ATP phosphoribosyltransferase	Busch et al. (2001, A. nidulans)	ANID	An13g01080	54800
r318	:	PRBATP + H_2O ⇒ PPI + PRBAMP	3.6.1.31	phosphoribosyl-ATP diphosphatase	Berlyn (1967), Busch et al. (2001, A. nidulans)	ANID	An01g12570	205513
r319	:	PRBAMP + H_2O ⇒ PRFP	3.5.4.19	phosphoribosyl-AMP cyclohydrolase	Berlyn (1967), Busch et al. (2001, A. nidulans)	ANID	An01g12570	205513
r320	:	PRFP ⇒ PRLP	5.3.1.16	1-(5-phosphoribosyl)-5-[(5-phosphoribosylamino)methylideneamino 4-carboxamide isomerase	Busch et al. (2001, A. nidulans)	ANID	An17g01640	51056
r321	:	PRLP + GLN ⇒ GLU + AICAR + DIMGP	2.4.2.-	Glutamine amidotransferase:cyclase/imidazole glycerol phosphate synthase	Valerius et al. (2001, A. nidulans)	ANID	An02g14890	198031
r322	:	DIMGP ⇒ IMACP + H_2O	4.2.1.19	Imidazoleglycerol-phosphate dehydratase	Berlyn (1967), Busch et al. (2001, A. nidulans)	ANID	An15g00610	200493
r323	:	IMACP + GLU ⇒ AKG + HISOLP	2.6.1.9	Histidinol-phosphate aminotransferase	Pain et al. (2004, A. fumigatus)	ANID	An01g11930	171507
r324	:	HISOLP + H_2O ⇒ PI + HISOL	3.1.3.15	Histidinol phosphatase		ANID	An14g00840	56528
r325	:	HISOL + 2 NAD + H_2O ⇒ HIS + 2 NADH	1.1.1.23	Histidinol dehydrogenase	Berlyn (1967), Creaser and Varela-Torres (1971, A. nidulans)	ANID	An14g07210	56640
Histidine degradation								
r326	:	HIS ⇒ HISN + CO_2	4.1.1.22	histidine decarboxylase	Tanaka et al. (1977)	ANEW		
r327	:	ACCOA + HISN ⇆ COA + NAHISN	No EC	histamine N-acetyltransferase	Tanaka et al. (1977)	ANEW		
Valine and leucine biosynthesis								
r328	:	2 PYRm ⇒ CO_2m + ACLACm	2.2.1.6	Acetolactate synthase		ANID	An01g09250; An03g00480; An16g01310; An16g04170	35805; 51385; 139646; 210558
r329	:	ACLACm + NADPHm ⇒ NADPm + DHVALm	1.1.1.86	Ketol-acid reductoisomerase		ANID	An09g03940	212581
r330	:	DHVALm ⇒ OIVALm + H_2Om	4.2.1.9	Dihydroxy acid dehydratase		ANID	An07g09870; An11g09270; An15g06700; An18g02550; An18g04160	181283; 179001; 53523; 42733; 54174
r331	:	OIVALm + GLUm ⇆ AKGm + VALm	2.6.1.42	Branched chain amino acid aminotransferase		ANEW	An12g02890; An02g06150; An04g00430; An09g01990	43811; 197362; 190990; 124698
r337	:	OIVALm + ACCOAm + H_2Om ⇒ COAm + IPPMALm	2.3.3.13	Alpha-isopropylmalate synthase (2-isopropylmalate synthase)		ANID	An01g13160; An09g00170	205459; 203189
r338	:	IPPMALm + NADm ⇒ NADHm + OICAPm + CO_2m	1.1.1.85	β-IPM (isopropylmalate) dehydrogenase (leu2A and leu2B)	Williams et al. (1996), Kohlhaw (2003)	ANID	An04g10130; An01g14130	205291; 205395
r339	:	OICAPm + GLUm ⇆ AKGm + LEUm	2.6.1.42	Branched chain amino acid aminotransferase		ANID	An12g02890; An02g06150; An04g00430; An09g01990	43811; 197362; 190990; 124698
r339m	:	OICAP + GLU ⇆ AKG + LEU	2.6.1.42	Branched chain amino acid aminotransferase		ANID	An12g02890; An02g06150; An04g00430; An09g01990	43811; 197362; 190990; 124698
Isoleucine biosynthesis								
r332	:	OBUTm + PYRm ⇒ ABUTm + CO_2m	2.2.1.6	Acetolactate synthase		ANID	An01g09250; An03g00480; An16g01310; An16g04170	35805; 51385; 139646; 210558
r333	:	ABUTm + NADPHm ⇒ NADPm + DHMVAm	1.1.1.86	Ketol-acid reductoisomerase		ANID	An09g03940	212581

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r334	:	DHMVAm ⇒ OMVALm + H_2Om	4.2.1.9	Dihydroxy acid dehydratase		ANID		An07g09870; An11g09270; An15g06700; An18g02550; An18g04160	181283; 179001; 53523; 42733; 54174
r335	:	OMVALm + GLUm ⇆ AKGm + ILEm	2.6.1.42	Branched chain amino acid amino-transferase		ANID		An12g02890; An02g06150; An04g00430; An09g01990	43811; 197362; 190990; 124698
r335m	:	OMVAL + GLU ⇆ AKG + ILE	2.6.1.42	Branched chain amino acid amino-transferase		ANID		An12g02890; An02g06150; An04g00430; An09g01990	43811; 197362; 190990; 124698
Lysine biosynthesis					Garrad and Bhattacharjee (1992, Fungi)				
r341	:	ACCOAm + H_2Om + AKGm ⇒ HCITm + COAm	2.3.3.14	Homocitrate synthase	Garrad and Bhattacharjee (1992, A. fumigatus)	ANID		An04g06210	54991
r351	:	HCITm ⇆ HACNm + H_2Om	4.2.1.79	2-methylcitrate dehydratase	Weidner et al. (1997, A. nidulans)	ANID		An15g01780	53423
r352	:	HACNm + H_2Om ⇆ HICITm	4.2.1.36	Homoaconitate hydratase	Weidner et al. (1997), Zabriskie and Jackson (2000, A. nidulans)	ANID		An15g00350	56275
r353	:	HICITm + NADm ⇆ OXAm + CO_2m + NADHm	1.1.1.87	Homoisocitrate dehydrogenase	Garrad and Bhattacharjee (1992, A. fumigatus), Zabriskie and Jackson (2000), Weidner et al. (1997, A. nidulans)	ANID			
NE3	:	OXAm ⇆ CO_2m + AKAm	Non enzymatic step	Non enzymatic reaction		ANID			
r346	:	AKAm + GLUm ⇆ AMAm + AKGm	2.6.1.39	2-aminoadipate transaminase	Garrad and Bhattacharjee (1992, A. fumigatus), Weidner et al. (1997), Zabriskie and Jackson (2000, A. nidulans)	ANID			
r347	:	AMAm + NADPHm ⇒ AMASAm + NADPm + H_2Om	1.2.1.31	L-aminoadipate-semialdehyde dehydrogenase	Garrad and Bhattacharjee (1992, A. fumigatus), Zabriskie and Jackson (2000, A. nidulans)	ANID		An04g05420; An11g04250; An12g10090; An11g05500	55018; 129526; 194895; 39114
r348	:	AMAm + NADHm ⇒ AMASAm + NADm + H_2Om	1.2.1.31	L-aminoadipate-semialdehyde dehydrogenase	Garrad and Bhattacharjee (1992, A. fumigatus), Zabriskie and Jackson (2000, A. nidulans)	ANID		An04g05420; An11g04250; An12g10090; An11g05500	55018; 129526; 194895; 39114
r349	:	GLUm + AMASAm + NADPHm ⇆ SACPm + NADPm + H_2Om	1.5.1.10	Saccharopine dehydrogenase ($NADP^+$, L-glutamate forming)	Garrad and Bhattacharjee (1992, A. fumigatus), Zabriskie and Jackson (2000, A. nidulans)	ANID		An01g13590; An04g05260	35485; 214383
r350	:	SACPm + NADm + H_2Om ⇆ LYSm + AKGm + NADHm	1.5.1.7	Saccharopine dehydrogenase (NAD+, L-lysine forming)	Garrad and Bhattacharjee (1992, A. fumigatus), Zabriskie and Jackson (2000, A. nidulans)	ANID		An02g07500	207003
Methionine metabolism									
r354	:	SAM + HCYS ⇒ SAH + MET	2.1.1.10	Homocysteine S-methyltransferase	Stepien et al. (1975, A. nidulans)	ANID		An15g07110	210376
r355	:	ACCOA + HSER ⇆ COA + OAHSER	2.3.1.31	homoserine O-acetyltransferase	Stepien et al. (1975), Sieńko and Paszewski (1999), Grynberg et al. (2001, A. nidulans)	ANID		An17g00630	213962
r356	:	OAHSER + CYS ⇆ LLCT + AC	2.5.1.48	Cystathionine gamma-synthase	Paszewski and Grabski (1975), Stepien et al. (1975), Sieńko and Paszewski (1999, A. nidulans)	ANEW		An12g01110	128744
r357	:	OAHSER + METH ⇆ MET + AC	2.5.1.49	O-acetylhomoserine (thiol)-lyase		ANID		An09g06710	54281
r358	:	OAHSER + H2S ⇒ AC + HCYS	2.5.1.47	Cysteine synthase (O-acetylhomoserine sulfhydrylase)	Pieniazek et al. (1974), Paszewski and Grabski (1975), Stepien et al. (1975), Sieńko and Paszewski (1999, A. nidulans)	ANID		An02g10750; An12g09880; An14g00960; An15g05170; An16g07520	207249; N/A; 184767; 181861; 193596
r359	:	HCYS + SER ⇒ LLCT + H_2O	4.2.1.22	Cystathionine β-synthase	Pieniazek et al. (1974), Paszewski and Grabski (1975), Stepien et al. (1975, A. nidulans)	ANEW		An05g00160	49760
r360	:	LLCT ⇒ CYS + NH_3 + OBUT	4.4.1.1	Cystathionine gamma-lyase	Pieniazek et al. (1974), Stepien et al. (1975), Sieńko and Paszewski (1999, A. nidulans)	ANID		An04g04720; An16g08720	190884; 194072
r361	:	LLCT + H_2O ⇒ HCYS + PYR + NH_3	4.4.1.8	Cystathionine-b-lyase	Stepien et al. (1975), Sieńko and Paszewski (1999, A. nidulans)	ANID		An14g00930	201388
r362	:	HCYS + MTHF ⇒ THF + MET	2.1.1.13	Methionine synthase	Balinska and Paszewski (1979), Paszewski and Grabski (1975, A. nidulans)	ANID		An04g01750	203669
r363	:	MET + ATP + H_2O ⇒ PPI + PI + SAM	2.5.1.6	S-adenosylmethionine synthetase	Martinelli and Kinghorn (1994, A. nidulans)	ANID	*	An02g10660; An08g02700	175387; 208283
r364	:	SAM + CALH ⇒ SAH + DPTH	2.1.1.98	Diphthine synthase	Martinelli and Kinghorn (1994, A. nidulans), Pain et al. (2004, A. fumigatus)	ANID		An08g07220	47429
r365	:	SAH + H_2O ⇒ HCYS + ADN	3.3.1.1	Adenosylhomocysteinase (S-adenosyl-l-homocysteine hydrolase)	David et al. (2003), Sieńko and Paszewski (1999, A. nidulans)	ANIG, ANID		An08g01960	208343
Phenylalanine, tyrosine and tryptophan biosynthesis (aromatic amino acids)									
r367	:	E4P + PEP + H_2O ⇒ PI + 3DDAH7P	2.5.1.54	3-deoxy-7-phosphoheptulonate synthase	Hartmann et al. (2001, A. nidulans)	ANID		An01g06150	196476

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r368	:	3DDAH7P ⇒ DQT + PI	4.2.3.4	Pentafunctional arom polypeptide (contains: 3-dehydroquinate synthase, 3-dehydroquinate dehydratase (3-dehydroquinase), shikimate 5-dehydrogenase, shikimate kinase, and EPSP synthase)	Hawkins (1987), Nichols et al. (2004, A. nidulans)	ANID	An08g06800; An08g06810	207929; 207929
r369	:	DQT ⇒ DHSK + H_2O	4.2.1.10	Catabolic 3-dehydroquinase (3-dehydroquinate dehydratase)	Cain (1972a)	ANID	An08g06800; An08g06810	207929; 207929
r370	:	QT + NAD ⇆ DQT + NADH	1.1.1.24	Quinate 5-dehydrogenase	Cain (1972a)	ANID	An03g03710; An04g08100	44404; 51457
r371	:	DHSK + NADH ⇒ SME + NAD	1.1.1.24	Quinate 5-dehydrogenase	Cain (1972a)	ANEW	An03g03710; An04g08100	44404; 51457
r372	:	DHSK + NADPH ⇒ SME + NADP	1.1.1.25	dehydroshikimate dehydrogenase	Cain (1972a)	ANID	An08g06800; An08g06810	207929; 207929
r373	:	SME + ATP ⇒ ADP + SME3P	2.7.1.71	Shikimate kinase I, II	Hawkins (1987, A. nidulans)	ANID	An08g06800; An08g06810	207929; 207929
r374	:	SME3P + PEP ⇒ 3PSME + PI	2.5.1.19	3-phosphoshikimate-1-carboxyvinyltransferase	Hawkins (1987, A. nidulans)	ANID	An08g06800; An08g06810	207929; 207929
r375	:	3PSME ⇒ PI + CHOR	4.2.3.5	Chorismate synthase	Martinelli and Kinghorn (1994, A. nidulans)	ANID		
r376	:	CHOR ⇒ PHEN	5.4.99.5	Chorismate mutase	Yelton et al. (1983), Krappmann et al. (1999, A. nidulans)	ANID	An14g06010	41927
r377	:	PHEN ⇒ CO_2 + H_2O + PHPYR	4.2.1.51	Prephenate dehydratase		ANID	An17g02200	54937
r378	:	PHPYR + GLU ⇆ AKG + PHE	2.6.1.1	Phenylalanine:alpha-ketoglutarate aminotransferase	Alvarez-Vasquez et al. (2000)	ANID	An03g00050; An03g01120; An04g05130; An04g06380; An09g02390; An12g07870; An16g05570	141281; 45764; 214397; 214270; 50187; 186098; 56390
r379	:	PHEN + NADP ⇒ 4HPP + CO_2 + NADPH	1.3.1.13	Prephenate dehydrogenase ($NADP^+$)		ANID	An02g06120	46999
r380	:	4HPP + GLU ⇆ AKG + TYR	2.6.1.1	Aspartate transaminase	Alvarez-Vasquez et al. (2000)	ANID	An03g00050; An03g01120; An04g05130; An04g06380; An09g02390; An12g07870; An16g05570	141281; 45764; 214397; 214270; 50187; 186098; 56390
r381	:	CHOR + GLN ⇒ GLU + PYR + AN	4.1.3.27	Anthranilate synthase (trpC)	Kos et al. (1985), Horng et al. (1989), Adams and Royer (1990)	ANID	An08g06080	52668
r382	:	AN + PRPP ⇒ PPI + NPRAN	2.4.2.18	Anthranilate phosphoribosyl transferase		ANID	An01g07260	51886
r383	:	NPRAN ⇒ CPAD5P	5.3.1.24	N-(5′-phosphoribosyl)-anthranilate isomerase (trpC)	Kos et al. (1985), Horng et al. (1989), Adams and Royer (1990)	ANID	An08g06080	52668
r384	:	CPAD5P ⇒ CO_2 + IGP + H_2O	4.1.1.48	Indoleglycerol phosphate synthase (trpC)	Kos et al. (1985), Horng et al. (1989), Adams and Royer (1990)	ANID	An08g06080	52668
r385	:	IGP + SER ⇒ T3P1 + TRP + H_2O	4.2.1.20	Tryptophan synthetase		ANID	An02g02170; An12g03230; An16g02500	52146; 43841; 183278
Proline biosynthesis								
r412	:	GLU + NADH ⇒ NAD + GLUGSAL + 2 H_2O	1.5.1.12	1-pyrroline-5-carboxylate dehydrogenase	Jones et al. (1981), Hull et al. (1989, A. nidulans)	ANEW	An02g02290; An07g05000; An11g06140	52149; 181275; 208879
NE4	:	GLUGSAL ⇆ P5C + H_2O	Non enzymatic step	Non enzymatic reaction		ANID		
r413	:	P5C + NADPH ⇆ PRO + NADP	1.5.1.2	Pyrroline-5-carboxylate reductase	Jones et al. (1981), Hull et al. (1989, A. nidulans)	ANID	An07g05050; An01g01520; An04g02800	136532; 36398; 57044
r414	:	GLU + ATP ⇒ ADP + GLUP	2.7.2.11	Gamma-glutamyl kinase, glutamate kinase		ANID	An05g00120	124391
r415	:	PROm + NADm ⇒ P5Cm + NADHm	1.5.99.8	Proline dehydrogenase		ANID	An01g01530; An11g06160	132598; 179947
NE5	:	GLUGSALm ⇆ P5Cm	Non enzymatic step	Non enzymatic reaction		ANID		
Proline degradation								
r416	:	P5C + NAD + 2 H_2O ⇒ GLU + NADH	1.5.1.12	1-pyrroline-5-carboxylate dehydrogenase	Jones et al. (1981), Hull et al. (1989, A. nidulans)	ANEW	An02g02290; An07g05000; An11g06140	52149; 181275; 208879

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
METABOLISM OF OTHER AMINO ACIDS						ANID		
Beta-alanine biosynthesis					Kanehisa et al. (2002), Jerebzoff and Jerebzoff-Quintin (1971)			
r417	:	ASP ⇒ CO_2 + bALA	4.1.1.11	Aspartate α-decarboxylase		ANID		
Cyanoamino acid metabolism								
r418	:	APROP ⇒ ALA + NH_3	3.5.5.1	Nitrilase	Snajdrova et al. (2004)	ANID	An16g00550; An01g07510; An01g12090; An06g01960; An08g08940; An08g10150; An12g01260; An16g06210; An18g01740	41410; 35944; 170270; 175987; N/A; 52578; 141873; 40928; 211815
r419	:	ACYBUT ⇒ GLU + NH_3	3.5.5.1	Nitrilase	Snajdrova et al. (2004)	ANID	An16g00550; An01g07510; An01g12090; An06g01960; An08g08940; An08g10150; An12g01260; An16g06210; An18g01740	41410; 35944; 170270; 175987; N/A; 52578; 141873; 40928; 211815
Glutathione biosynthesis								
r420	:	CYS + GLU + ATP ⇒ GC + PI + ADP	6.3.2.2	Gamma-glutamylcysteine synthetase		ANID	An08g01270	38585
r421	:	GLY + GC + ATP ⇒ RGT + PI + ADP	6.3.2.3	Glutathione synthetase	Murata et al. (1989)	ANID	An01g13620; An09g03030	170255; 50166
r422	:	OGT + O_2 ⇒ RGT + H_2O_2	1.11.1.9	Glutathione peroxidase	Vignaud et al. (2002), Kuzniak et al. (2006)	ANID	An02g02750	206591
r423	:	NADPH + OGT ⇒ NADP + RGT	1.8.1.7	glutathione-disulfide reductase		ANID	An03g03660	213429
NUCLEOTIDE METABOLISM						ANID		
Purine Biosynthesis (ATP, dATP, IMP, XMP, GTP, dGTP)					Foley et al. (1965, A. nidulans)			
r424	:	PRPP + GLN + H_2O ⇒ PPI + GLU + PRAM	2.4.2.14	Phosphoribosylpyrophosphate amidotransferase/amidophosphoribosyltransferase	Foley et al. (1965, A. nidulans)	ANID	An15g01760	129349
r425	:	PRAM + ATP + GLY ⇆ ADP + PI + GAR	6.3.4.13	Glycinamide ribotide synthetase and aminoimidazole ribotide synthetase/phosphoribosylamine-glycine ligase	Foley et al. (1965, A. nidulans)	ANID	An15g00570	53390
r426	:	GAR + FTHF ⇒ THF + FGAR	2.1.2.2	Phosphoribosylglycinamide formyltransferase	Foley et al. (1965, A. nidulans)	ANID	An02g02700	36764
r427	:	FGAR + ATP + GLN + H_2O ⇒ GLU + ADP + PI + FGAM	6.3.5.3	5′-phosphoribosylformylglycinamidine synthetase	Foley et al. (1965, A. nidulans)	ANID	An02g09960	37283
r428	:	FGAM + ATP ⇒ ADP + PI + AIR	6.3.3.1	Phosphoribosylformylglycinamide cyclo-ligase	Foley et al. (1965, A. nidulans)	ANID	An15g00570	53390
r429	:	AIR + CO_2 ⇆ CAIR	4.1.1.21	Phosphoribosylaminoimidazole carboxylase (Ade2 homolog)	Jin et al. (2004, A. oryzae)	ANID	An01g08090	55358
r430	:	CAIR + ATP + ASP ⇒ ADP + PI + SAICAR	6.3.2.6	Phosphoribosyl amino imidazolesuccinocarbozamide synthetase (Ade1 homolog)	Jin et al. (2004, A. oryzae)	ANID	An11g10150	48145
r431	:	SAICAR ⇆ FUM + AICAR	4.3.2.2	5′-phosphoribosyl-4-(N-succinocarboxamide)-5-aminoimidazole lyase	Jin et al. (2004, A. oryzae)	ANID	An02g04020	206692
r432	:	AICAR + FTHF ⇆ THF + PRFICA	2.1.2.3	5-aminoimidazole-4-carboxamide ribonucleotide (AICAR) transformylase / IMP cyclohydrolase	Jin et al. (2004, A. oryzae)	ANID	An04g02060	57068
r433	:	PRFICA ⇆ IMP + H_2O	3.5.4.10	5-aminoimidazole-4-carboxamide ribonucleotide (AICAR) transformylase / IMP cyclohydrolase	Jin et al. (2004, A. oryzae)	ANID	An04g02060	57068
r434	:	IMP + GTP + ASP ⇒ GDP + PI + ASUC	6.3.4.4	Adenylosuccinate synthetase	Foley et al. (1965), Ribard et al. (2001, A. nidulans)	ANID	An01g13920	51711
r435	:	ASUC ⇒ FUM + AMP	4.3.2.2	5′-phosphoribosyl-4-(N-succinocarboxamide)-5-aminoimidazole lyase	Foley et al. (1965), Ribard et al. (2001, A. nidulans)	ANID	An02g04020	206692
r436	:	ATP + AMP ⇆ 2 ADP	2.7.4.3	Adenylate kinase	Perl (1982)	ANIG, ANID	An01g04710; An07g10100	46678; 56109

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r437	:	ADP + RTHIO ⇒ DADP + OTHIO + H_2O	1.17.4.1	Ribonucleotide reductase	Hockertz et al. (1987)	ANID	*	An04g01080; An14g06870	57102; 56635
r438	:	DAMP + ATP ⇆ DADP + ADP	2.7.4.11	Adenylate kinase, dAMP kinase		ANID		An01g04710	46678
r439	:	DADP + ATP ⇆ DATP + ADP	2.7.4.6	Nucleoside-diphosphate kinase	Lin et al. (2003, A. nidulans)	ANID		An09g05870	212435
r440	:	IMP + NAD ⇒ NADH + XMP	1.1.1.205	Inosine-5′-monophosphate dehydrogenase		ANID		An07g08170	53197
r441	:	XMP + ATP + GLN + H_2O ⇒ GLU + AMP + PPI + GMP	6.3.5.2	GMP synthase		ANID		An02g14520	37616
r442	:	GMP + ATP ⇆ GDP + ADP	2.7.4.8	Guanylate kinase		ANID		An01g07070; An08g00300	143052; 130364
r443	:	GDP + ATP ⇆ GTP + ADP	2.7.4.6	Nucleoside-diphosphate kinase	Lin et al. (2003, A. nidulans), David et al. (2003)	ANIG, ANID		An09g05870	212435
r444	:	GTP + AMP ⇆ ADP + GDP	2.7.4.3	Adenylate kinase	Perl (1982)	ANIG, ANID		An01g04710; An07g10100	46678; 56109
r445	:	GDP + RTHIO ⇒ DGDP + OTHIO + H_2O	1.17.4.1	Ribonucleotide reductase	Hockertz et al. (1987)	ANID	*	An04g01080; An14g06870	57102; 56635
r446	:	DGDP + ATP ⇆ DGTP + ADP	2.7.4.6	Nucleoside-diphosphate kinase	Lin et al. (2003, A. nidulans)	ANID		An09g05870	212435
r447	:	DGDP + ADP ⇆ DGMP + ATP	2.7.4.8	Guanylate kinase		ANID		An01g07070; An08g00300	143052; 130364
r448	:	ITP + AMP ⇆ ADP + IDP	2.7.4.6	Adenylate kinase	Perl (1982)	ANIG, ANID		An09g05870	212435
r449	:	IDP + H_2O ⇒ IMP + PI	3.6.1.6	Inosine diphosphatase		ANID			
Purine conversions									
r450	:	GMP + DATP ⇆ GDP + DADP	2.7.4.8	Guanylate kinase		ANID		An01g07070; An08g00300	143052; 130364
Purine degradation					Darlington et al. (1965), Scazzocchio et al. (1982, A. nidulans), Kanehisa et al. (2002), Elzainy et al. (1989)				
r451	:	AMP + H_2O ⇒ PI + ADN	3.1.3.5	5′-nucleotidase	Kuwahara and Fujii (1978), Elzainy et al. (1989), Elzainy and Ali (2000), Ali and Elzainy (2000)	ANID		An08g08080	128775
r452	:	AMP + H_2O ⇆ AD + R5P	3.2.2.4	AMP nucleosidase	Kuwahara and Fujii (1978)	ANEW			
r453	:	ADN + H_2O ⇒ AD + RIB	3.2.2.1	Purine nucleoside hydrolase	Kuwahara and Fujii (1978), Elzainy et al. (1978, 1989)	ANID		An08g03980	55818
r454	:	ADN + H_2O ⇒ INS + NH_3	3.5.4.4	Adenosine deaminase	Ribard et al. (2003, A. nidulans), Mitschell and McElroy (1946), Grosshans and Wolfenden (1993, A. oryzae), Abu-Shady et al. (1994, A. terricola)	ANID		An12g04800; An16g02890	49658; 183577
r455	:	AD + H_2O ⇒ NH_3 + HYXN	3.5.4.2	Adenine deaminase	Scazzocchio et al. (1982), Ribard et al. (2001, A. nidulans)	ANID		An12g04800; An16g02890	49658; 183577
r456	:	DAMP + H_2O ⇒ DA + PI	3.1.3.5	5′-nucleotidase	Rama and Shanmugasundaram (1985, A. nidulans)	ANID		An08g08080	128775
r457	:	DA + PI ⇆ AD + DR1P	2.4.2.1	Purine nucleotide phosphorylase, xanthosine phosphorylase		ANID		An11g06110	178461
r458	:	DA + H_2O ⇒ DIN + NH_3	3.5.4.4	Adenine deaminase/adenosine deaminase	Ribard et al. (2003, Inferred), Grosshans and Wolfenden (1993, A. oryzae)	ANID		An12g04800; An16g02890	49658; 183577
r459	:	DIN + PI ⇆ HYXN + DR1P	2.4.2.1	Purine nucleotide phosphorylase, xanthosine phosphorylase		ANID		An11g06110	178461
r460	:	IMP + H_2O ⇒ PI + INS	3.1.3.5	5′-nucleotidase	Kuwahara and Fujii (1978)	ANID		An08g08080	128775
r461	:	IMP + H_2O ⇒ HYXN + R5P	3.2.2.1	purine nucleosidase	Kuwahara and Fujii (1978)	ANEW		An08g03980	55818
r462	:	INS + PI ⇒ HYXN + R1P	2.4.2.1	Purine nucleotide phosphorylase, xanthosine phosphorylase	Kuwahara and Fujii (1978), Elzainy et al. (1978)	ANID		An11g06110	178461
r463	:	INS + H_2O ⇒ HYXN + RIB	3.2.2.1	Purine nucleosidase/purine nucleoside hydrolase	Kuwahara and Fujii (1978), Elzainy et al. (1978)	ANEW		An08g03980	55818
r464	:	HYXN + NAD + H_2O ⇆ XAN + NADH	1.17.1.4	Xanthine dehydrogenase	Darlington et al. (1965), Scazzocchio et al. (1982, A. nidulans)	ANEW		An03g01530	214667
r465	:	GMP + H_2O ⇒ PI + GSN	3.1.3.5	5′-nucleotidase	Elzainy et al. (1989), Ali and Elzainy (2000)	ANID		An08g08080	128775
r466	:	GSN + PI ⇆ GN + R5P	3.2.2.1	purine nucleosidase	Kuwahara and Fujii (1978)	ANEW		An08g03980	55818
r467	:	GSN + H_2O ⇒ GN + RIB	3.2.2.1	Purine nucleosidase/purine nucleoside hydrolase	Kuwahara and Fujii (1978), Elzainy et al. (1978, 1989)	ANID		An08g03980	55818
r468	:	GN + H_2O ⇆ XAN + NH_3	3.5.4.3	Guanine aminohydrolase	Darlington et al. (1965, Inferred)	ANEW		An11g01070; An14g01140	38774; 184651

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r469	:	DGMP + H_2O ⇒ DG + PI	3.1.3.5	5′-nucleotidase	Rama and Shanmugasundaram (1985, A. nidulans)	ANID		An08g08080	128775
r470	:	DG + PI ⇆ GN + DR1P	2.4.2.1	Purine nucleotide phosphorylase, xanthosine phosphorylase		ANID		An11g06110	178461
r471	:	XMP + H_2O ⇒ PI + XTSINE	3.1.3.5	5′-nucleotidase	Rama and Shanmugasundaram (1985, A. nidulans)	ANID		An08g08080	128775
r472	:	PI + XTSINE ⇆ XAN + R1P	2.4.2.1	Purine nucleotide phosphorylase, xanthosine phosphorylase		ANID		An11g06110	178461
r473	:	XAN + NAD + H_2O ⇆ URIC + NADH	1.17.1.4	Xanthine dehydrogenase (purine hydroxylase I)	Darlington et al. (1965), Arst and Cove (1969), Scazzocchio et al. (1982, A. nidulans)	ANEW		An03g01530	214667
r474	:	URIC + O_2 + H_2O ⇆ HIUR + H_2O_2	1.7.3.3	Uricase	Ertan and Aksoz (2000)	ANEW		An02g06030; An03g02330	55563; 51359
r475	:	HIUR + H_2O ⇒ ATN + CO_2	3.5.2.17	Hydroxyisourate hydrolase + spontaneous conversion	Darlington et al. (1965, A. nidulans)	ANEW			
r476	:	ATN + H_2O ⇆ ATT	3.5.2.5	Allantoinase	Darlington et al. (1965), Arst and Cove (1969), Scazzocchio et al. (1982, A. nidulans)	ANID		An14g03370	N/A
r477	:	ATT + H_2O ⇆ UGC + UREA	3.5.3.4	Allantoicase	Darlington et al. (1965), Arst and Cove (1969), Scazzocchio et al. (1982, A. nidulans)	ANID		An02g08520	172988
r478	:	UGC + H_2O ⇒ GLX + 2 NH_3 + CO_2	3.5.3.19	Ureidoglycolate hydrolase	Darlington et al. (1965, A. nidulans)	ANID		An16g08100	193909
Pyrimidine biosynthesis (UTP, CTP, dCTP, dUTP and dTTP)					Evans and Guy (2004), Kanehisa et al. (2002)				
r479	:	GLN + 2 ATP + CO_2 + 2 H_2O ⇒ GLU + CAP + 2 ADP + PI	6.3.5.5	Carbamoyl-phosphate synthetase, aspartate transcarbamylase, and glutamine amidotransferase	Palmer et al. (1975), Aleksenko et al. (1999, A. nidulans)	ANID	*	An16g04960; An16g04970; An17g00820	53574; 53574; 54890
r480	:	CAP + ASP ⇒ CAASP + PI	2.1.3.2	Aspartate-carbamoyltransferase	Palmer et al. (1975, A. nidulans)	ANID		An08g07420	55738
r481	:	CAASP ⇆ DOROA + H_2O	3.5.2.3	Dihydroorotase		ANID		An01g10650; An08g07420	205639; 55738
r482	:	DOROA + O_2 ⇒ H_2O_2 + OROA	1.3.3.1	Dihydroorotate dehydrogenase	Gustafson and Waldron (1992, A. nidulans)	ANID		An02g02910	36779
r483	:	OROA + PRPP ⇆ PPI + OMP	2.4.2.10	Orotate phosphoribosyltransferase 1		ANID		An04g08330	55173
r484	:	OMP ⇒ CO_2 + UMP	4.1.1.23	Orotidine-5′-phosphate decarboxylase (pyrA)	Goosen et al. (1987)	ANID		An12g03570	56726
r485	:	ADP + UDP ⇆ ATP + UMP	2.7.4.14	Cytidylate kinase		ANID		An13g00440	50815
r486	:	UTP + AMP ⇆ UDP + ADP	2.7.4.3	Adenylate kinase	David et al. (2003)	ANIG		An01g04710; An07g10100	46678; 56109
r487	:	UDP + ATP ⇆ UTP + ADP	2.7.4.6	Nucleoside-diphosphate kinase	Lin et al. (2003, A. nidulans), David et al. (2003)	ANIG, ANID		An09g05870	212435
r488	:	UTP + GLN + ATP + H_2O ⇒ GLU + CTP + ADP + PI	6.3.4.2	CTP synthase		ANID		An03g01310	57431
r489	:	ATP + UTP + NH_3 ⇒ ADP + PI + CTP	6.3.4.2	CTP synthase		ANID		An03g01310	57431
r490	:	CTP + ADP ⇆ CDP + ATP	2.7.4.6	Nucleoside-diphosphate kinase	Lin et al. (2003, A. nidulans), David et al. (2003)	ANIG, ANID		An09g05870	212435
r491	:	CTP + AMP ⇆ CDP + ADP	2.7.4.3	Adenylate kinase	David et al. (2003)	ANIG		An01g04710; An07g10100	46678; 56109
r492	:	ADP + CDP ⇆ CMP + ATP	2.7.4.14	Cytidylate kinase		ANID		An13g00440	50815
r493	:	CDP + RTHIO ⇒ DCDP + OTHIO + H_2O	1.17.4.1	Ribonucleotide reductase, small subunit (alt), β chain	Hockertz et al. (1987)	ANID	*	An04g01080; An14g06870	57102; 56635
r494	:	UDP + RTHIO ⇒ OTHIO + DUDP + H_2O	1.17.4.1	Ribonucleotide reductase, small subunit (alt), β chain	Hockertz et al. (1987)	ANID	*	An04g01080; An14g06870	57102; 56635
r495	:	DUMP + METTHF ⇒ DHF + DTMP	2.1.1.45	Thymidylate synthase		ANID		An14g00570	49219
r496	:	DCDP + ATP ⇆ DCTP + ADP	2.7.4.6	Nucleoside-diphosphate kinase	Lin et al. (2003, A. nidulans)	ANID		An09g05870	212435
r497	:	DCMP + ATP ⇆ ADP + DCDP	2.7.4.14	Nucleoside-phosphate kinase/ATP:UMP-CMP phosphotransferase/cytidylate kinase		ANID		An13g00440	50815
r498	:	DUDP + ATP ⇆ DUTP + ADP	2.7.4.6	Nucleoside-diphosphate kinase	Lin et al. (2003, A. nidulans)	ANID		An09g05870	212435
r499	:	DUMP + ATP ⇆ DUDP + ADP	2.7.4.9	Uridylate kinase		ANID		An09g05840	56895
r500	:	DTMP + ATP ⇆ ADP + DTDP	2.7.4.9	dTMP kinase/thymidylate kinase		ANID		An09g05840	56895
r501	:	DTDP + ATP ⇆ DTTP + ADP	2.7.4.6	Nucleoside-diphosphate kinase	Lin et al. (2003, A. nidulans)	ANID		An09g05870	212435
Pyrimidine conversions									
r502	:	URI + GTP ⇒ UMP + GDP	2.7.1.48	Uridine kinase		ANID		An11g09320	53035
r503	:	URI + ATP ⇒ ADP + UMP	2.7.1.48	Uridine kinase		ANID		An11g09320	53035
r504	:	CYTD + GTP ⇒ GDP + CMP	2.7.1.48	Uridine kinase		ANID		An11g09320	53035

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r505	:	URA + PRPP ⇒ UMP + PPI	2.4.2.9	UPRTase, uracil phosphoribosyltransferase (furA)		ANID	An12g09660; An12g09670; An15g06580; An17g02370	42030; 49490; 53518; 54952
r506	:	DUTP + H_2O ⇒ PPI + DUMP	3.6.1.23	dUTP pyrophosphatase (dUTPase)		ANID	An01g05040	172313
r507	:	DOROA + Qm ⇒ QH_2m + OROA	1.3.1.14	Dihydroorotate dehydrogenase	Gustafson and Waldron (1992), Aleksenko et al. (1999, A. nidulans)	ANID	An02g02910	36779
r508	:	OTHIO + NADPH ⇒ NADP + RTHIO	1.8.1.9	Thioredoxin reductase		ANID	An12g02850	50359
r509	:	OTHIOm + NADPHm ⇒ NADPm + RTHIOm	1.8.1.9	Thioredoxin reductase		ANID	An12g02850	50359
Pyrimidine degradation					Darlington et al. (1965, A. nidulans), Kanehisa et al. (2002), Elzainy et al. (1989)			
r510	:	UMP + H_2O ⇒ PI + URI	3.1.3.5	5′-nucleotidase	Ali and Elzainy (2000)	ANID	An08g08080	128775
r511	:	URI + H_2O ⇒ URA + RIB	3.2.2.3	Uridine hydrolase	Fukami (1961, A. nidulans)	ANEW	An18g04340	42881
r512	:	CMP + H_2O ⇒ CYTD + PI	3.1.3.5	5′-nucleotidase	Elzainy et al. (1989), Ali and Elzainy (2000)	ANID	An08g08080	128775
r513	:	CYTD + H_2O ⇒ URI + NH_3	3.5.4.5	Cytidine deaminase	Elzainy et al. (1989), Ali (1998)	ANID	An03g06870	50782
r514	:	CMP + H_2O ⇒ CYTS + R5P	3.2.2.10	CMP glycosylase		ANID		
r515	:	CYTS + H_2O ⇒ URA + NH_3	3.5.4.1	Cytosine deaminase	Fukami (1961, A. nidulans)	ANID	An01g04260	206127
r516	:	DCMP + H_2O ⇒ DC + PI	3.1.3.5	5′-nucleotidase	Rama and Shanmugasundaram (1985, A. nidulans)	ANID	An08g08080	128775
r517	:	DC + H_2O ⇒ NH_3 + DU	3.5.4.5	Deoxycytidine deaminase	Fukami (1961, A. nidulans)	ANID	An03g06870	50782
r518	:	DUMP + H_2O ⇒ DU + PI	3.1.3.5	5′-nucleotidase	Rama and Shanmugasundaram (1985, A. nidulans)	ANID	An08g08080	128775
r519	:	URA + DR1P ⇒ DU + PI	2.4.2.1	Purine-nucleoside phosphorylase		ANEW	An11g06110	178461
r520	:	DTMP + H_2O ⇒ DT + PI	3.1.3.5	5′-nucleotidase	Rama and Shanmugasundaram (1985, A. nidulans)	ANID	An08g08080	128775
r521	:	THY + DR1P ⇒ DT + PI	2.4.2.1	Purine-nucleoside phosphorylase		ANEW	An11g06110	178461
Salvage pathways for nucleotides								
r522	:	HYXN + PRPP ⇒ PPI + IMP	2.4.2.8	Hypoxanthine phosphoribosyltransferase		ANID	An14g00280	210854
r523	:	GN + PRPP ⇒ PPI + GMP	2.4.2.8	Hypoxanthine phosphoribosyltransferase		ANID	An14g00280	210854
r524	:	AD + PRPP ⇒ PPI + AMP	2.4.2.7	Adenine phosphoribosyltransferase	Ribard et al. (2001, A. nidulans)	ANID	An12g00320	54445
r525	:	XAN + PRPP ⇒ XMP + PPI	2.4.2.22	Xanthine-guanine phosphoribosyltransferase		ANID	An14g00280	210854
r526	:	PRPP + H_2O ⇒ PRCP + PI	No EC	Non Enz	Trembacz and Jezewska (1990)	ANEW		
r527	:	PRCP + H_2O ⇒ R1P + PI	No EC	Non Enz	Trembacz and Jezewska (1990)	ANEW		
r528	:	AD + R1P ⇒ PI + ADN	2.4.2.1	Purine nucleotide phosphorylase, xanthosine phosphorylase		ANID		
r529	:	GN + R1P ⇒ PI + GSN	2.4.2.1	Purine nucleotide phosphorylase, xanthosine phosphorylase		ANID		
r531	:	ADN + ATP ⇒ AMP + ADP	2.7.1.20	Adenosine kinase	David et al. (2003)	ANIG, ANID	An17g01330	214022
r532	:	INS + ATP ⇒ IMP + ADP	2.7.1.73	Inosine kinase		ANID		
r533	:	GSN + ATP ⇒ GMP + ADP	2.7.1.73	Inosine kinase		ANID		
r534	:	ATP ⇒ cAMP + PPI	4.6.1.1	Adenylate cyclase	Wold and Suzuki (1974)	ANID	An11g01520	178015
r535	:	cAMP ⇒ AMP	3.1.4.17	3′,5′-cyclic-nucleotide phosphodiesterase	Wold and Suzuki (1974), Pall (1981)	ANID	An01g04450; An01g13010	36176; 195992
r536	:	cdAMP ⇒ DAMP	3.1.4.17	3′,5′-cyclic-nucleotide phosphodiesterase		ANID	An01g04450; An01g13010	36176; 195992
r537	:	cIMP ⇒ IMP	3.1.4.17	3′,5′-cyclic-nucleotide phosphodiesterase		ANID	An01g04450; An01g13010	36176; 195992
r538	:	cGMP ⇒ GMP	3.1.4.17	3′,5′-cyclic-nucleotide phosphodiesterase, low affinity		ANID	An01g04450; An01g13010	36176; 195992
r539	:	cCMP ⇒ CMP	3.1.4.17	3′,5′-cyclic-nucleotide phosphodiesterase, low affinity		ANID	An01g04450; An01g13010	36176; 195992
r540	:	cAMPe ⇒ AMPe	3.1.4.17	3′,5′-cyclic-nucleotide phosphodiesterase	Wold and Suzuki (1974)	ANEW	An01g04450; An01g13010	36176; 195992
r541	:	ATPm + AMPm ⇆ 2 ADPm	2.7.4.3	Adenylate kinase		ANIG, ANID	An01g04710; An07g10100	46678; 56109

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r542	:	GTPm + AMPm ⇆ ADPm + GDPm	2.7.4.3	Adenylate kinase		ANIG, ANID	An01g04710; An07g10100	46678; 56109
r543	:	ITPm + AMPm ⇆ ADPm + IDPm	2.7.4.3	Adenylate kinase		ANID	An01g04710; An07g10100	46678; 56109
NAD and NADPH metabolism					Kuwahara and Fujii (1978), Kuwahara et al. (1982, 1983)			
Nicotinate and Nicotinamide biosynthesis					Kuwahara and Fujii (1978), Kuwahara et al. (1983)			
r544	:	ASP + O_2 ⇒ IMASP + H_2O_2	1.4.3.16	L-aminoacid oxidase	Sarma et al. (1962, Inferred)	ANEW		
r1267	:	IMASP + T3P1 ⇆ QUIN + 2 H_2O + PI	No Ec	quinolinate synthetase, NadA	Sarma et al. (1962, Inferred)	ANEW		
r545	:	QUIN + PRPP ⇒ NAMN + PPI + CO_2	2.4.2.19	Nicotinate mononucleotide pyrophosphorylase	Sarma et al. (1962, Inferred)	ANEW	An11g10910	56085
r546	:	NICD + H_2O ⇆ NICA + NH_3	3.5.1.19	nicotinamidase	Sarma et al. (1964), Kuwahara et al. (1983)	ANEW	An07g08360	48305
r547	:	NICA + PRPP ⇒ NAMN + PPI	2.4.2.11	Nicotinate phosphoribosyltransferase	Sarma et al. (1962), Kuwahara et al. (1983, Inferred)	ANEW	An12g00760	50290
r548	:	ATP + NAMN ⇒ PPI + DMNAD	2.7.7.1	Nicotinamide-nucleotide adenylyltransferase	Kuwahara et al. (1983, Inferred)	ANEW	An11g06610	178093
r549	:	ATP + DMNAD + GLN + H_2O ⇆ AMP + PPI + NAD + GLU	6.3.5.1	NAD synthetase	Kuwahara et al. (1983, Inferred)	ANEW	An09g05660	54326
r550	:	ATP + NAD ⇒ ADP + NADP	2.7.1.23	NAD kinase	Kuwahara et al. (1982, Inferred)	ANEW	An03g05090; An14g06430	191587; 53896
NADP and NAD degradation					Kuwahara and Fujii (1978), Kuwahara et al. (1983), Elzainy and Ali (2000)			
r551	:	NADP + H_2O ⇒ NAD + PI	No EC	NADPH phosphatase	Kuwahara et al. (1982, Inferred)	ANEW		
r552	:	NAD + H_2O ⇒ NAMR + ADP	No EC	acid phosphatase	Elzainy and Ali (2000)	ANEW		
r553	:	NAD + H_2O ⇒ ADPR + NICD	3.2.2.5	NAD-glycohydrolase	Sarma et al. (1964),	ANEW		
r554	:	NAD + H_2O ⇒ AMP + NMN	3.6.1.22	NAD pyrophosphatase	Kuwahara et al. (1983, Inferred)	ANEW	An09g05670	212451
r555	:	NMN + H_2O ⇒ NAMR + PI	3.1.3.5	5′-nucleotidase	Kuwahara et al. (1983, Inferred)	ANEW	An08g08080	128775
r556	:	NAMR + H_2O ⇒ NAR + NH_3	No EC	nicotinate nucleotide amidase	Kuwahara et al. (1983)	ANEW		
r557	:	NMN + H_2O ⇆ R5P + NICD	3.2.2.14	NMN nucleosidase	Kuwahara et al. (1983, Inferred)	ANEW		
r558	:	NAMN + H_2O ⇒ NAR + PI	3.1.3.5	5′-nucleotidase	Kuwahara et al. (1982, 1983, Inferred) Snajdrova et al. (2004)	ANEW	An08g08080	128775
3-Cyanopyridine degradation								
r1213	:	3CPYRD + 2 H_2O ⇒ NICA + NH_3	3.5.5.1	benzonitrilase	Snajdrova et al. (2004)	ANEW	An16g00550; An01g07510; An01g12090; An06g01960; An08g08940; An08g10150; An12g01260; An16g06210; An18g01740	41410; 35944; 170270; 175987; N/A; 52578; 141873; 40928; 211815
LIPID METABOLISM								
FATTY ACIDS METABOLISM								
Formation of saturated cytosolic fatty acids (Even numbers)								
r559	:	CBCCP + ACCOA ⇆ BCCP + MALCOA	6.4.1.2	Acetyl-CoA carboxylase (ACC) / biotin carboxylase	Schwenk and Bennett (1969)	ANID	An12g04020	56715
r560	:	ATP + BCCP + CO_2 + H_2O ⇆ ADP + PI + CBCCP	6.3.4.14	Biotin carboxylase	Schwenk and Bennett (1969)	ANEW	An12g04020	56715
r561	:	MALCOA + ACP ⇆ MALACP + COA	2.3.1.39	Malonyl transferase		ANEW	An04g00040	190484
r562	:	ACCOA + ACP ⇆ ACACP + COA	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r563	:	ACACP + MALACP ⇒ AACACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW	An02g14220; An14g01760	55650; 41604
r564	:	AACACP + NADPH ⇆ C4HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW	An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r565	:	C4HACP ⇆ C4DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r566	:	C4DACP + NADPH ⇆ C40ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r568	:	C40ACP + MALACP ⇒ C6OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r569	:	C6OACP + NADPH ⇆ C6HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r570	:	C6HACP ⇆ C6DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r571	:	C6DACP + NADPH ⇆ C60ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r573	:	C60ACP + MALACP ⇒ C8OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r574	:	C8OACP + NADPH ⇆ C8HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r575	:	C8HACP ⇆ C8DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r576	:	C8DACP + NADPH ⇆ C80ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r578	:	C80ACP + MALACP ⇒ C10OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r579	:	C10OACP + NADPH ⇆ C10HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r580	:	C10HACP $\leftrightarrows$ C10DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r581	:	C10DACP + NADPH $\leftrightarrows$ C100ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r583	:	C100ACP + MALACP $\Rightarrow$ C12OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r584	:	C12OACP + NADPH $\leftrightarrows$ C12HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r585	:	C12HACP $\leftrightarrows$ C12DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r586	:	C12DACP + NADPH $\leftrightarrows$ C120ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r588	:	C120ACP + MALACP $\Rightarrow$ C14OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r589	:	C14OACP + NADPH $\leftrightarrows$ C14HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An01g14000; An03g02840; An05g02050; An06g02000; An06g02610; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An16g07090; An18g00290	35566; 172477; 45652; 43929; 37709 and 47218; 137016; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 45606; 187979
r590	:	C14HACP $\leftrightarrows$ C14DACP + H_2O	4.2.1.61	Long chain β-hydroxypalmitoyl thioester dehydratase		ANEW		An12g01990	43740
r591	:	C14DACP + NADPH $\leftrightarrows$ C140ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r598	:	C140ACP + MALACP $\Rightarrow$ C16OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r599	:	C16OACP + NADPH ⇆ C16HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW	An01g12400; An01g14000; An03g02840; An05g02050; An06g02000; An06g02610; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An16g07090; An18g00290	35566; 172477; 45652; 43929; 37709 and 47218; 137016; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 45606; 187979
r600	:	C16HACP ⇆ C16DACP + H_2O	4.2.1.61	Long chain β-hydroxypalmitoyl thioester dehydratase		ANEW	An12g01990	43740
r601	:	C16DACP + NADPH ⇆ C160ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW	An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r608	:	C160ACP + MALACP ⇒ C18OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW	An02g14220; An14g01760	55650; 41604
r609	:	C18OACP + NADPH ⇆ C18HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW	An01g12400; An01g14000; An03g02840; An05g02050; An06g02000; An06g02610; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An16g07090; An18g00290	35566; 172477; 45652; 43929; 37709 and 47218; 137016; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 45606; 187979
r610	:	C18HACP ⇆ C18DACP + H_2O	4.2.1.61	Long chain β-hydroxypalmitoyl thioester dehydratase		ANEW	An12g01990	43740
r611	:	C18DACP + NADPH ⇆ C180ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW	An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r618	:	C180ACP + MALACP ⇒ C20OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW	An02g14220; An14g01760	55650; 41604
r619	:	C20OACP + NADPH ⇆ C20HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW	An01g12400; An01g14000; An03g02840; An05g02050; An06g02000; An06g02610; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An16g07090; An18g00290	35566; 172477; 45652; 43929; 37709 and 47218; 137016; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 45606; 187979
r620	:	C20HACP ⇆ C20DACP + H_2O	4.2.1.61	Long chain β-hydroxypalmitoyl thioester dehydratase		ANEW	An12g01990	43740

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r621	:	C20DACP + NADPH ⇆ C200ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
Formation of saturated cytosolic fatty acids (Odd numbers)									
r1224	:	PROPCOA + ACP ⇆ PROPACP + COA	2.3.1.38	[ACP]acetyltransferase		ANEW		An12g01990	43740
r1225	:	PROPACP + MALACP ⇒ C5OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r1226	:	C5OACP + NADPH ⇆ C5HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r1227	:	C5HACP ⇆ C5DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r1228	:	C5DACP + NADPH ⇆ C50ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r1230	:	C50ACP + MALACP ⇒ C7OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r1231	:	C7OACP + NADPH ⇆ C7HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r1232	:	C7HACP ⇆ C7DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r1233	:	C7DACP + NADPH ⇆ C70ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r1235	:	C70ACP + MALACP ⇒ C9OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r1236	:	C9OACP + NADPH ⇆ C9HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r1237	:	C9HACP ⇆ C9DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r1238	:	C9DACP + NADPH ⇆ C90ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r1240	:	C90ACP + MALACP ⇒ C11OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r1241	:	C11OACP + NADPH ⇆ C11HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r1242	:	C11HACP ⇆ C11DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r1243	:	C11DACP + NADPH ⇆ C110ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r1245	:	C110ACP + MALACP ⇒ C13OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r1246	:	C13OACP + NADPH ⇆ C13HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r1247	:	C13HACP ⇆ C13DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r1248	:	C13DACP + NADPH ⇆ C130ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r1250	:	C130ACP + MALACP ⇒ C15OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r1251	:	C15OACP + NADPH ⇆ C15HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r1252	:	C15HACP ⇆ C15DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r1253	:	C15DACP + NADPH ⇆ C150ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r1255	:	C150ACP + MALACP ⇒ C17OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r1256	:	C17OACP + NADPH ⇆ C17HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r1257	:	C17HACP ⇆ C17DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r1258	:	C17DACP + NADPH ⇆ C170ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
r1260	:	C170ACP + MALACP ⇒ C19OACP + CO_2 + ACP	2.3.1.41	3-oxoacyl-[acyl-carrier-protein] synthase		ANEW		An02g14220; An14g01760	55650; 41604
r1261	:	C19OACP + NADPH ⇆ C19HACP + NADP	1.1.1.100	3-oxoacyl-[acyl-carrier-protein] reductase		ANEW		An01g12400; An03g02840; An05g02050; An06g02000; An08g01930; An11g00760; An12g02320; An12g05100; An13g01130; An14g01270; An14g06740; An18g00290	35566; 45652; 43929; 37709 and 47218; 177736; 124830; 189865; 49639; 44744; 124614; 185180; 187979
r1262	:	C19HACP ⇆ C19DACP + H_2O	2.3.1.85	Fatty-acid synthase		ANEW	*	An08g10930; An09g02010; An12g01980	47227; 188253; 189622
r1263	:	C19DACP + NADPH ⇆ C190ACP + NADP	1.3.1.9	Enoyl-ACP reductase		ANEW		An07g03290; An16g05340; An04g02300	209754; 56395; 190311
Formation of unsaturated cytosolic fatty acids					Chattopadhyay et al. (1985b,a)				
r623	:	C190ACP + NADH + O_2 ⇆ C191ACP + NAD + 2 H_2O	1.14.19.1	C190-CoA 9-desaturase	Chattopadhyay et al. (1985b)	ANEW		An07g01960; An12g09940	209875; 195065
r624	:	C191ACP + NADH + O_2 ⇆ C192ACP + NAD + 2 H_2O	1.14.19.3	C190-CoA 12-desaturase	Chattopadhyay et al. (1985a)	ANEW		An07g06770; An16g06350	209561; 48908
r625	:	C180ACP + NADH + O_2 ⇆ C181ACP + NAD + 2 H_2O	1.14.19.1	stearoyl-CoA 9-desaturase	Chattopadhyay et al. (1985b)	ANEW		An07g01960; An12g09940	209875; 195065
r626	:	C181ACP + NADH + O_2 ⇆ C182ACP + NAD + 2 H_2O	1.14.19.3	stearoyl-CoA 12-desaturase	Chattopadhyay et al. (1985a)	ANEW		An07g06770; An16g06350	209561; 48908
r627	:	C182ACP + NADH + O_2 ⇆ C183ACP + NAD + 2 H_2O	No EC	stearoyl-CoA 15-desaturase	Chattopadhyay et al. (1985a)	ANEW			
r988	:	C170ACP + NADH + O_2 ⇆ C171ACP + NAD + 2 H_2O	No EC	C170-CoA 9-desaturase	Levery et al. (2000, Inferred)	ANEW			
r628	:	C160ACP + NADH + O_2 ⇆ C161ACP + NAD + 2 H_2O	1.14.19.1	C160-CoA 9-desaturase	Chattopadhyay et al. (1985b, Inferred)	ANEW		An07g01960; An12g09940	209875; 195065
r629	:	C161ACP + NADH + O_2 ⇆ C162ACP + NAD + 2 H_2O	1.14.19.3	C160-CoA 12-desaturase	Chattopadhyay et al. (1985a, Inferred)	ANEW		An07g06770; An16g06350	209561; 48908
r630	:	C140ACP + NADH + O_2 ⇆ C141ACP + NAD + 2 H_2O	1.14.19.1	C160-CoA 9-desaturase	Chattopadhyay et al. (1985a, Inferred)	ANEW		An07g01960; An12g09940	209875; 195065
Removal of ACPs									
r936	:	C40ACP + H_2O ⇒ C40 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW			
r937	:	C60ACP + H_2O ⇒ C60 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW			
r938	:	C80ACP + H_2O ⇒ C80 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW			

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r939	:	C100ACP + H_2O ⇒ C100 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r940	:	C120ACP + H_2O ⇒ C120 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r941	:	C140ACP + H_2O ⇒ C140 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r942	:	C141ACP + H_2O ⇒ C141 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r943	:	C150ACP + H_2O ⇒ C150 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r944	:	C160ACP + H_2O ⇒ C160 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r945	:	C161ACP + H_2O ⇒ C161 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r946	:	C162ACP + H_2O ⇒ C162 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r947	:	C170ACP + H_2O ⇒ C170 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r987	:	C171ACP + H_2O ⇒ C171 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r948	:	C180ACP + H_2O ⇒ C180 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r949	:	C181ACP + H_2O ⇒ C181 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r950	:	C182ACP + H_2O ⇒ C182 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r951	:	C183ACP + H_2O ⇒ C183 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r952	:	C190ACP + H_2O ⇒ C190 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r953	:	C191ACP + H_2O ⇒ C191 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r954	:	C192ACP + H_2O ⇒ C192 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
r955	:	C200ACP + H_2O ⇒ C200 + ACP	3.1.2.14	Acyl-ACP-hydrolase		ANEW		
Transfer of ACP-Acyls to COA for transport and biosynthesis								
r631	:	C40ACP + COA ⇆ C40COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r617	:	C40ACP + COA ⇆ C40COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW		
r632	:	C60ACP + COA ⇆ C60COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r633	:	C80ACP + COA ⇆ C80COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r634	:	C100ACP + COA ⇆ C100COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r635	:	C120ACP + COA ⇆ C120COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r636	:	C140ACP + COA ⇆ C140COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r637	:	C141ACP + COA ⇆ C141COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r638	:	C150ACP + COA ⇆ C150COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r639	:	C160ACP + COA ⇆ C160COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r640	:	C161ACP + COA ⇆ C161COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r641	:	C162ACP + COA ⇆ C162COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r642	:	C170ACP + COA ⇆ C170COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r985	:	C171ACP + COA ⇆ C171COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r643	:	C180ACP + COA ⇆ C180COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r644	:	C181ACP + COA ⇆ C181COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r645	:	C182ACP + COA ⇆ C182COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r646	:	C183ACP + COA ⇆ C183COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r647	:	C190ACP + COA ⇆ C190COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r648	:	C191ACP + COA ⇆ C191COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r649	:	C192ACP + COA ⇆ C192COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
r650	:	C200ACP + COA ⇆ C200COA + ACP	2.3.1.38	[ACP]acetyltransferase		ANEW	An12g01990	43740
Transfer of Acyls to COA for transport and biosynthesis								
r651	:	C40 + COA + ATP ⇒ C40COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An18g03800	187366
r652	:	C60 + COA + ATP ⇒ C60COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An18g03800	187366
r653	:	C80 + COA + ATP ⇒ C80COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An18g03800	187366
r654	:	C100 + COA + ATP ⇒ C100COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An18g03800	187366
r655	:	C120 + COA + ATP ⇒ C120COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An18g03800; An09g06740	187366; 188673
r656	:	C140 + COA + ATP ⇒ C140COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An18g03800; An09g06740	187366; 188673
r657	:	C141 + COA + ATP ⇒ C141COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An18g03800; An09g06740	187366; 188673
r658	:	C150 + COA + ATP ⇒ C150COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An18g03800; An09g06740	187366; 188673
r659	:	C160 + COA + ATP ⇒ C160COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r660	:	C161 + COA + ATP ⇒ C161COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r661	:	C162 + COA + ATP ⇒ C162COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r662	:	C170 + COA + ATP ⇒ C170COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r986	:	C171 + COA + ATP ⇒ C171COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r663	:	C180 + COA + ATP ⇒ C180COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r664	:	C181 + COA + ATP ⇒ C181COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r665	:	C182 + COA + ATP ⇒ C182COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r666	:	C183 + COA + ATP ⇒ C183COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r667	:	C190 + COA + ATP ⇒ C190COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r668	:	C191 + COA + ATP ⇒ C191COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r669	:	C192 + COA + ATP ⇒ C192COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
r670	:	C200 + COA + ATP ⇒ C200COA + PPI + AMP	6.2.1.3	Acyl-CoA synthetase	Baltazar et al. (1999)	ANEW	An09g06740	188673
Fatty acids conversions					Kanehisa et al. (2002)			

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r671	:	2 ACCOA ⇆ COA + AACCOA	2.3.1.9	Acetyl-CoA C-acetyltransferase, acetoacetyl-CoA thiolase		ANID	An16g09190	214441
r672	:	ACTAC + ATP + COA ⇆ ADP + AACCOA + PI	6.4.1.2, 6.3.4.14	Acetyl-CoA carboxylase (ACC) / biotin carboxylase	Inferred for ACTAC connection	ANEW		
Fa ac de da tio					Baltazar et al. (1999)			
Carnitine shuttle								
r678	:	C120COA + CAR ⇆ COA + C120CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r679	:	C140COA + CAR ⇆ COA + C140CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r680	:	C141COA + CAR ⇆ COA + C141CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r681	:	C150COA + CAR ⇆ COA + C150CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r682	:	C160COA + CAR ⇆ COA + C160CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r683	:	C161COA + CAR ⇆ COA + C161CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r684	:	C162COA + CAR ⇆ COA + C162CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r685	:	C170COA + CAR ⇆ COA + C170CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r1211	:	C171COA + CAR ⇆ COA + C171CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r686	:	C180COA + CAR ⇆ COA + C180CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r687	:	C181COA + CAR ⇆ COA + C181CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r688	:	C182COA + CAR ⇆ COA + C182CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r689	:	C183COA + CAR ⇆ COA + C183CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r690	:	C190COA + CAR ⇆ COA + C190CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r691	:	C191COA + CAR ⇆ COA + C191CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r692	:	C192COA + CAR ⇆ COA + C192CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r693	:	C200COA + CAR ⇆ COA + C200CAR	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r699	:	CARm + C120CAR ⇒ CAR + C120CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r700	:	CARm + C140CAR ⇒ CAR + C140CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r701	:	CARm + C141CAR ⇒ CAR + C141CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r702	:	CARm + C150CAR ⇒ CAR + C150CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r703	:	CARm + C160CAR ⇒ CAR + C160CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r704	:	CARm + C161CAR ⇒ CAR + C161CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r705	:	CARm + C162CAR ⇒ CAR + C162CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r706	:	CARm + C170CAR ⇒ CAR + C170CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r989	:	CARm + C171CAR ⇒ CAR + C171CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r707	:	CARm + C180CAR ⇒ CAR + C180CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r708	:	CARm + C181CAR ⇒ CAR + C181CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r709	:	CARm + C182CAR ⇒ CAR + C182CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r710	:	CARm + C183CAR ⇒ CAR + C183CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r711	:	CARm + C190CAR ⇒ CAR + C190CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r712	:	CARm + C191CAR ⇒ CAR + C191CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r713	:	CARm + C192CAR ⇒ CAR + C192CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r714	:	CARm + C200CAR ⇒ CAR + C200CARm		Carnitine transport reaction	Jernejc and Legisa (1996)	ANEW		
r720	:	C120CARm + COAm ⇆ CARm + C120COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r721	:	C140CARm + COAm ⇆ CARm + C140COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r722	:	C141CARm + COAm ⇆ CARm + C141COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r723	:	C150CARm + COAm ⇆ CARm + C150COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r724	:	C160CARm + COAm ⇆ CARm + C160COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r725	:	C161CARm + COAm ⇆ CARm + C161COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r726	:	C162CARm + COAm ⇆ CARm + C162COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r727	:	C170CARm + COAm ⇆ CARm + C170COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r990	:	C171CARm + COAm ⇆ CARm + C171COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r728	:	C180CARm + COAm ⇆ CARm + C180COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r729	:	C181CARm + COAm ⇆ CARm + C181COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r730	:	C182CARm + COAm ⇆ CARm + C182COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r731	:	C183CARm + COAm ⇆ CARm + C183COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r732	:	C190CARm + COAm ⇆ CARm + C190COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r733	:	C191CARm + COAm ⇆ CARm + C191COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r734	:	C192CARm + COAm ⇆ CARm + C192COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
r735	:	C200CARm + COAm ⇆ CARm + C200COAm	2.3.1.7	Carnitine O-acetyltransferase	Jernejc and Legisa (1996), Baltazar et al. (1999)	ANEW	An08g04990; An18g01590	198577; 120926
Oxidation of fatty acids (even numbers)								
r736	:	C200COAm + FADm ⇒ C20DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r737	:	C200COAm + FADm ⇒ C20DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r738	:	C20DCOAm + H_2Om ⇆ C20HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r739	:	C20HCOAm + NADm ⇆ C20OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r740	:	C20OCOAm + COAm ⇒ ACCOAm + C180COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r746	:	C180COAm + FADm ⇒ C18DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r747	:	C180COAm + FADm ⇒ C18DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r748	:	C18DCOAm + H_2Om ⇆ C18HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r749	:	C18HCOAm + NADm ⇆ C18OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r750	:	C18OCOAm + COAm ⇒ ACCOAm + C160COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r756	:	C160COAm + FADm ⇒ C16DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r757	:	C160COAm + FADm ⇒ C16DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r758	:	C16DCOAm + H_2Om ⇆ C16HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r759	:	C16HCOAm + NADm ⇆ C16OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r760	:	C16OCOAm + COAm ⇒ ACCOAm + C140COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r766	:	C140COAm + FADm ⇒ C14DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r767	:	C140COAm + FADm ⇒ C14DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r768	:	C14DCOAm + H_2Om ⇆ C14HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r769	:	C14HCOAm + NADm ⇆ C14OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r770	:	C14OCOAm + COAm ⇒ ACCOAm + C120COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r771	:	C120COAm + FADm ⇒ C12DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r772	:	C120COAm + FADm ⇒ C12DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r773	:	C12DCOAm + H_2Om ⇆ C12HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r774	:	C12HCOAm + NADm ⇆ C12OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r775	:	C12OCOAm + COAm ⇒ ACCOAm + C100COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r776	:	C100COAm + FADm ⇒ C10DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r777	:	C100COAm + FADm ⇒ C10DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r778	:	C10DCOAm + H_2Om ⇆ C10HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r779	:	C10HCOAm + NADm ⇆ C10OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r780	:	C10OCOAm + COAm ⇒ ACCOAm + C80COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r781	:	C80COAm + FADm ⇒ C8DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r782	:	C80COAm + FADm ⇒ C8DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r783	:	C8DCOAm + H_2Om ⇆ C8HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r784	:	C8HCOAm + NADm ⇆ C8OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r785	:	C8OCOAm + COAm ⇒ ACCOAm + C60COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r786	:	C60COAm + FADm ⇒ C6DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r787	:	C6DCOAm + H_2Om ⇆ C6HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r788	:	C6HCOAm + NADm ⇆ C6OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r789	:	C6OCOAm + COAm ⇒ ACCOAm + C40COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r790	:	C40COAm + FADm ⇒ C4DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Kazimirova and Novotelnov (1956, Inferred)	ANEW	An17g01150	128861
r791	:	C4DCOAm + H_2Om ⇆ C4HCOAm	4.2.1.17	Enoyl-CoA hydratase	Kazimirova and Novotelnov (1956, Inferred)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r792	:	C4HCOAm + NADm ⇆ AACCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Kazimirova and Novotelnov (1956, Inferred)	ANEW	An14g00990; An12g03260	201398; 43844
r793	:	AACCOAm + COAm ⇒ 2 ACCOAm	2.3.1.9	Acetyl-CoA C-acetyltransferase, acetoacetyl-CoA thiolase		ANEW	An13g01920	44808
Oxidation of fatty acids (odd chains)								
r741	:	C190COAm + FADm ⇒ C19DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r742	:	C190COAm + FADm ⇒ C19DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r743	:	C19DCOAm + H_2Om ⇆ C19HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r744	:	C19HCOAm + NADm ⇆ C19OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r745	:	C19OCOAm + COAm ⇒ ACCOAm + C170COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r751	:	C170COAm + FADm ⇒ C17DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r752	:	C170COAm + FADm ⇒ C17DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r753	:	C17DCOAm + H_2Om ⇆ C17HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r754	:	C17HCOAm + NADm ⇆ C17OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r755	:	C17OCOAm + COAm ⇒ ACCOAm + C150COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r761	:	C150COAm + FADm ⇒ C15DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r762	:	C150COAm + FADm ⇒ C15DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r763	:	C15DCOAm + H_2Om ⇆ C15HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r764	:	C15HCOAm + NADm ⇆ C15OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r765	:	C15OCOAm + COAm ⇒ ACCOAm + C130COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r593	:	C130COAm + FADm ⇒ C13DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r594	:	C130COAm + FADm ⇒ C13DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r595	:	C13DCOAm + H_2Om ⇆ C13HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r596	:	C13HCOAm + NADm ⇆ C13OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r597	:	C13OCOAm + COAm ⇒ ACCOAm + C110COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r603	:	C110COAm + FADm ⇒ C11DCOAm + FADH2m	1.3.99.13	Long-chain-acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An04g03290; An13g03940	57034; 191914
r604	:	C110COAm + FADm ⇒ C11DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r605	:	C11DCOAm + H_2Om ⇆ C11HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r606	:	C11HCOAm + NADm ⇆ C11OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r607	:	C11OCOAm + COAm ⇒ ACCOAm + C90COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r613	:	C90COAm + FADm ⇒ C9DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r614	:	C9DCOAm + H_2Om ⇆ C9HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r615	:	C9HCOAm + NADm ⇆ C9OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r616	:	C9OCOAm + COAm ⇒ ACCOAm + C70COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r673	:	C70COAm + FADm ⇒ C7DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r674	:	C7DCOAm + H_2Om ⇆ C7HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r675	:	C7HCOAm + NADm ⇆ C7OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r676	:	C7OCOAm + COAm ⇒ ACCOAm + C50COAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
r694	:	C50COAm + FADm ⇒ C5DCOAm + FADH2m	1.3.99.3	Acyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An17g01150	128861
r695	:	C5DCOAm + H_2Om ⇆ C5HCOAm	4.2.1.17	Enoyl-CoA hydratase	Baltazar et al. (1999)	ANEW	An14g00990; An02g02820; An02g05840; An02g07320	201398; 36773; N/A; 197480
r696	:	C5HCOAm + NADm ⇆ C5OCOAm + NADHm	1.1.1.35	3-hydroxyacyl-CoA dehydrogenase	Baltazar et al. (1999)	ANEW	An14g00990; An12g03260	201398; 43844
r697	:	C5OCOAm + COAm ⇒ ACCOAm + PROPCOAm	2.3.1.16	3-ketoacyl-CoA thiolase	Baltazar et al. (1999)	ANEW	An02g03320; An04g05720; An08g05400; An13g00590	46947; 55007; 38275; 50823
PHOSPHOLIPID BIOSYNTHESIS					Chopra and Khuller (1984), Kanehisa et al. (2002)			
Phosphatidylserine								
r794	:	GL3P + 0.022 C120ACP + 0.031 C140ACP + 0.022 C141ACP + 0.214 C160ACP + 0.045 C161ACP + 0.016 C162ACP + 0.045 C170ACP + 0.08 C180ACP + 0.2 C181ACP + 0.183 C182ACP + 0.081 C183ACP + 0.061 C200ACP ⇒ PSAGL3P + ACP	2.3.1.15	Glycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An18g01960	188006
r795	:	T3P2 + 0.022 C120ACP + 0.031 C140ACP + 0.022 C141ACP + 0.214 C160ACP + 0.045 C161ACP + 0.016 C162ACP + 0.045 C170ACP + 0.08 C180ACP + 0.2 C181ACP + 0.183 C182ACP + 0.081 C183ACP + 0.061 C200ACP ⇒ PSAT3P2 + ACP	2.3.1.15	Glycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An18g01960	188006

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r796	:	PSAT3P2 + NADPH ⇒ PSAGL3P + NADP	1.1.1.101	Acyldihydroxyacetonephosphate reductase/ acylglycerone-phosphate reductase	Chopra and Khuller (1984, Inferred)	ANID	An16g06470	184098
r797	:	PSAGL3P + 0.022 C120ACP + 0.031 C140ACP + 0.022 C141ACP + 0.214 C160ACP + 0.045 C161ACP + 0.016 C162ACP + 0.045 C170ACP + 0.08 C180ACP + 0.2 C181ACP + 0.183 C182ACP + 0.081 C183ACP + 0.061 C200ACP ⇒ PSPA + ACP	2.3.1.51	1-acylglycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An13g00040	126602
r798	:	PSPA + CTP ⇆ PSCDPDG + PPI	2.7.7.41	Cdp-diacylglycerol synthetase (phosphatidate cytidylyltransferase)	Chopra and Khuller (1984, Inferred)	ANID	An07g09570	181254
r799	:	PSCDPDG + SER ⇆ CMP + PS	2.7.8.8	Phosphatidylserine synthase	Chopra and Khuller (1984, Inferred)	ANID	An17g01120	51030
Phosphatidylethanolamine								
r800	:	GL3P + 0.03 C120ACP + 0.015 C140ACP + 0.011 C141ACP + 0.001 C150ACP + 0.24 C160ACP + 0.046 C161ACP + 0.039 C162ACP + 0.041 C170ACP + 0.093 C180ACP + 0.135 C181ACP + 0.282 C182ACP + 0.065 C183ACP + 0.002 C200ACP ⇒ PEAGL3P + ACP	2.3.1.15	Glycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An18g01960	188006
r801	:	T3P2 + 0.03 C120ACP + 0.015 C140ACP + 0.011 C141ACP + 0.001 C150ACP + 0.24 C160ACP + 0.046 C161ACP + 0.039 C162ACP + 0.041 C170ACP + 0.093 C180ACP + 0.135 C181ACP + 0.282 C182ACP + 0.065 C183ACP + 0.002 C200ACP ⇒ PEAT3P2 + ACP	2.3.1.15	Glycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An18g01960	188006
r802	:	PEAT3P2 + NADPH ⇒ PEAGL3P + NADP	1.1.1.101	Acyldihydroxyacetonephosphate reductase/ acylglycerone-phosphate reductase	Chopra and Khuller (1984, Inferred)	ANID	An16g06470	184098
r803	:	PEAGL3P + 0.03 C120ACP + 0.015 C140ACP + 0.011 C141ACP + 0.001 C150ACP + 0.24 C160ACP + 0.046 C161ACP + 0.039 C162ACP + 0.041 C170ACP + 0.093 C180ACP + 0.135 C181ACP + 0.282 C182ACP + 0.065 C183ACP + 0.002 C200ACP ⇒ PEPA + ACP	2.3.1.51	1-acylglycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An13g00040	126602
r804	:	PEPA + CTP ⇆ PECDPDG + PPI	2.7.7.41	Cdp-diacylglycerol synthetase (phosphatidate cytidylyltransferase)	Chopra and Khuller (1984, Inferred)	ANID	An07g09570	181254
r805	:	PECDPDG + SER ⇆ CMP + PEPS	2.7.8.8	Phosphatidylserine synthase	Chopra and Khuller (1984, Inferred)	ANID	An17g01120	51030
r806	:	PEPS ⇒ PE + CO_2	4.1.1.65	Phosphatidylserine decarboxylase	Chopra and Khuller (1984, Inferred)	ANID	An03g02830; An01g14110; An04g10280; An09g04710; An12g00910; An14g01880	194479; 35440; N/A; 202968; 50299; 41614
Phosphatidylcholine								
r807	:	GL3P + 0.01 C120ACP + 0.044 C140ACP + 0.077 C141ACP + 0.224 C160ACP + 0.039 C161ACP + 0.018 C162ACP + 0.048 C170ACP + 0.068 C180ACP + 0.131 C181ACP + 0.308 C182ACP + 0.021 C183ACP + 0.012 C200ACP ⇒ PCAGL3P + ACP	2.3.1.15	Glycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An18g01960	188006
r808	:	T3P2 + 0.01 C120ACP + 0.044 C140ACP + 0.077 C141ACP + 0.224 C160ACP + 0.039 C161ACP + 0.018 C162ACP + 0.048 C170ACP + 0.068 C180ACP + 0.131 C181ACP + 0.308 C182ACP + 0.021 C183ACP + 0.012 C200ACP ⇒ PCAT3P2 + ACP	2.3.1.15	Glycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An18g01960	188006
r809	:	PCAT3P2 + NADPH ⇒ PCAGL3P + NADP	1.1.1.101	Acyldihydroxyacetonephosphate reductase/ acylglycerone-phosphate reductase	Chopra and Khuller (1984, Inferred)	ANID	An16g06470	184098
r810	:	PCAGL3P + 0.01 C120ACP + 0.044 C140ACP + 0.077 C141ACP + 0.224 C160ACP + 0.039 C161ACP + 0.018 C162ACP + 0.048 C170ACP + 0.068 C180ACP + 0.131 C181ACP + 0.308 C182ACP + 0.021 C183ACP + 0.012 C200ACP ⇒ PCPA + ACP	2.3.1.51	1-acylglycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An13g00040	126602
r811	:	PCPA + CTP ⇆ PCCDPDG + PPI	2.7.7.41	Cdp-diacylglycerol synthetase (phosphatidate cytidylyltransferase)	Chopra and Khuller (1984, Inferred)	ANID	An07g09570	181254
r812	:	PCCDPDG + SER ⇆ CMP + PCPS	2.7.8.8	Phosphatidylserine synthase	Chopra and Khuller (1984, Inferred)	ANID	An17g01120	51030
r813	:	PCPS ⇒ PCPE + CO_2	4.1.1.65	Phosphatidylserine decarboxylase	Chopra and Khuller (1984, Inferred)	ANID	An03g02830; An01g14110; An04g10280; An09g04710; An12g00910; An14g01880	194479; 35440; N/A; 202968; 50299; 41614

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r814	:	PCPE + SAM ⇒ SAH + PCPMME	2.1.1.17	Phosphatidylethanolamine N-methyltransferase		ANID	An15g06310	53511
r815	:	PCPMME + SAM ⇒ SAH + PCPDME	2.1.1.71	Methylene-fatty-acyl-phospholipid synthase		ANID	An08g00560	208474
r816	:	PCPDME + SAM ⇒ PC + SAH	2.1.1.71	Methylene-fatty-acyl-phospholipid synthase		ANID	An08g00560	208474
Cardiolipin								
r817	:	GL3P + 0.024 C120ACP + 0.032 C140ACP + 0.017 C141ACP + 0.232 C160ACP + 0.027 C161ACP + 0.009 C162ACP + 0.017 C170ACP + 0.081 C180ACP + 0.124 C181ACP + 0.326 C182ACP + 0.111 C183ACP ⇒ CLAGL3P + ACP	2.3.1.15	Glycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An18g01960	188006
r818	:	CLAGL3P + 0.024 C120ACP + 0.032 C140ACP + 0.017 C141ACP + 0.232 C160ACP + 0.027 C161ACP + 0.009 C162ACP + 0.017 C170ACP + 0.081 C180ACP + 0.124 C181ACP + 0.326 C182ACP + 0.111 C183ACP ⇒ CLPA + ACP	2.3.1.51	1-acylglycerol-3-phosphate acyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An13g00040	126602
r819	:	CLPA + CTP ⇆ CLCDPDG + PPI	2.7.7.41	Cdp-diacylglycerol synthetase (phosphatidate cytidylyltransferase)	Chopra and Khuller (1984, Inferred)	ANID	An07g09570	181254
r820	:	CLCDPDG + GL3P ⇒ CMP + CLPIGP	2.7.8.5	CDP-diacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An17g01120	51030
r821	:	CLPIGP + H_2O ⇒ PG + PI	3.1.3.27	Phosphatidylglycerophosphatase	Chopra and Khuller (1984, Inferred)	ANID		
r822	:	CLCDPDG + PG ⇒ CMP + CL	CRD1	Cardiolipin synthase/CDP-diacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase	Chopra and Khuller (1984, Inferred)	ANID	An15g01020	126969
PHOSPHOLIPID DEGRADATION					Chopra and Khuller (1984), Kanehisa et al. (2002)	ANIG, ANID		
r823	:	PC ⇒ LPC + 0.01 C120 + 0.044 C140 + 0.077 C141 + 0.224 C160 + 0.039 C161 + 0.018 C162 + 0.048 C170 + 0.068 C180 + 0.131 C181 + 0.308 C182 + 0.021 C183 + 0.012 C200	3.1.1.4	Phospholipase A2/lecithinase a/phosphatidase/phosphatidolipase/phospholipase A	Mustranta et al. (1995)	ANID	An02g04040; An04g03360; An08g08490; An08g12250; An12g06690	52198; 44084; 176070; N/A; N/A
			3.1.1.32	Phospholipase B	Memon et al. (1983)		An15g05710	56347
r824	:	PE ⇒ LPE + 0.03 C120 + 0.015 C140 + 0.011 C141 + 0.001 C150 + 0.24 C160 + 0.046 C161 + 0.039 C162 + 0.041 C170 + 0.093 C180 + 0.135 C181 + 0.282 C182 + 0.065 C183 + 0.002 C200	3.1.1.4	Phospholipase a2/lecithinase A/phosphatidase/phosphatidolipase/phospholipase a		ANID	An02g04040; An04g03360; An08g08490; An08g12250; An12g06690	52198; 44084; 176070; N/A; N/A
			3.1.1.32	Phospholipase B	Memon et al. (1983)		An15g05710	56347
GLYCOSPHINGOLIPID METABOLISM					Kanehisa et al. (2002)			
Biosynthesis of precursors								
r825	:	G6P ⇆ MI1P	5.5.1.4	Myo-inositol-1-phosphate synthase		ANID	An10g00530	54854
r826	:	MI1P ⇒ MYOI + PI	3.1.3.25	Myo-inositol-1(or 4)-monophosphatase	Neuwald et al. (1991, A. nidulans)	ANID	An03g03700	54687
r827	:	0.25 CLCDPDG + 0.25 PCCDPDG + 0.25 PECDPDG + 0.25 PSCDPDG ⇒ CDPDG	No EC	Artificial reaction for TGDMIPC		ANEW		
r828	:	CDPDG + MYOI ⇒ CMP + PINS	2.7.8.11	Phosphatidylinositol synthase	Chopra and Khuller (1984, Inferred)	ANID	An01g14140	55234
r829	:	ATP + PINS ⇒ ADP + PINSP	2.7.1.137	1-phosphatidylinositol 3-kinase/phosphoinositide 3-kinase	Ibrahim-Granet et al. (2003, A. fumigatus)	ANID	An07g04820; An16g04720	39962; 53581
r830	:	C160COA + SER ⇒ COA + C18DHSPH + CO_2	2.3.1.50	Serine C-palmitoyltransferase	Mandala et al. (1994, A. fumigatus)	ANID	An08g04100; An18g03820	208165; 202464
r831	:	C18DHSPH + NADPH ⇒ C18SPH + NADP	1.1.1.102	3-dehydrosphinganine reductase		ANID	An01g06830	51907
r832	:	C18SPH + O_2 + NADPH ⇒ C18PSPH + NADP + H_2O	SUR2	Sphingosine hydroxylase/ syringomycin response protein 2		ANID	An01g10030	51801
r833	:	C180COA + SER ⇒ COA + C20DHSPH + CO_2	2.3.1.50	Serine C-palmitoyltransferase	Mandala et al. (1994, A. fumigatus)	ANEW	An08g04100; An18g03820	208165; 202464
r834	:	C20DHSPH + NADPH ⇒ C20SPH + NADP	1.1.1.102	3-dehydrosphinganine reductase		ANEW	An01g06830	51907
r835	:	C20SPH + O_2 + NADPH ⇒ C20PSPH + NADP + H_2O	SUR2	Sphingosine hydroxylase/ syringomycin response protein 2		ANEW	An01g10030	51801
r836	:	C171COA + SER ⇒ COA + C191DHSPH + CO_2	2.3.1.50	Serine C-palmitoyltransferase	Mandala et al. (1994, A. fumigatus)	ANEW	An08g04100; An18g03820	208165; 202464
r837	:	C191DHSPH + NADPH ⇒ C191SPH + NADP	1.1.1.102	3-dehydrosphinganine reductase		ANEW	An01g06830	51907
Biosynthesis of Cerebrin 1					Wagner and Fiegert (1969), Kanehisa et al. (2002)			
r838	:	C18PSPH + C180COA ⇒ CERB1A + COA	2.3.1.24	Ceramide synthase	Wagner and Fiegert (1969, Inferred)	ANEW	An11g00990	52868
r839	:	C18PSPH + C181COA ⇒ CERB1B + COA	2.3.1.24	Ceramide synthase	Wagner and Fiegert (1969, Inferred)	ANEW	An11g00990	52868

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r840	:	C20PSPH + C180COA ⇒ CERB1C + COA	2.3.1.24	Ceramide synthase	Wagner and Fiegert (1969, Inferred)	ANEW		An11g00990	52868
r841	:	C20PSPH + C181COA ⇒ CERB1D + COA	2.3.1.24	Ceramide synthase	Wagner and Fiegert (1969, Inferred)	ANEW		An11g00990	52868
r842	:	0.25 CERB1A + 0.25 CERB1B + 0.25 CERB1C + 0.25 CERB1D ⇒ CERB1	NO EC	Artificial reaction		ANEW			
Biosynthesis of Cerebrin 2					Wagner and Fiegert (1969), Kanehisa et al. (2002)				
r843	:	C18SPH + C180COA ⇒ CERB2A + COA	2.3.1.24	Ceramide synthase	Wagner and Fiegert (1969, Inferred)	ANEW		An11g00990	52868
r844	:	C18SPH + C181COA ⇒ CERB2B + COA	2.3.1.24	Ceramide synthase	Wagner and Fiegert (1969, Inferred)	ANEW		An11g00990	52868
r845	:	C20SPH + C180COA ⇒ CERB2C + COA	2.3.1.24	Ceramide synthase	Wagner and Fiegert (1969, Inferred)	ANEW		An11g00990	52868
r846	:	C20SPH + C181COA ⇒ CERB2D + COA	2.3.1.24	Ceramide synthase	Wagner and Fiegert (1969, Inferred)	ANEW		An11g00990	52868
r847	:	0.25 CERB2A + 0.25 CERB2B + 0.25 CERB2C + 0.25 CERB2D ⇒ CERB2	NO EC	Artificial reaction		ANEW			
Biosynthesis of Galactocerebroside					Wagner and Fiegert (1969), Kanehisa et al. (2002)				
r848	:	UDPGAL + CERB2A ⇒ UDP + GALCERA	2.4.1.45	2-hydroxyacylsphingosine 1-beta-galactosyltransferase	Wagner and Fiegert (1969, Inferred)	ANEW		An04g08370	45922
r849	:	UDPGAL + CERB2B ⇒ UDP + GALCERB	2.4.1.45	2-hydroxyacylsphingosine 1-beta-galactosyltransferase	Wagner and Fiegert (1969, Inferred)	ANEW		An04g08370	45922
r850	:	0.5 GALCERA + 0.5 GALCERB ⇒ GALCER	NO EC	Artifical reaction		ANEW			
Biosynthesis of Glucocerebroside 1					Levery et al. (2000), Kanehisa et al. (2002)	ANEW			
r851	:	C191SPH + C180COA ⇒ CEREB1 + COA	2.3.1.24	Ceramide synthase	Levery et al. (2000, Inferred)	ANEW		An11g00990	52868
r852	:	UDPG + CEREB1 ⇒ UDP + GLUCER1	2.4.1.80	2-hydroxyacylsphingosine 1-beta-glucosyltransferase	Levery et al. (2000, Inferred)	ANEW		An07g03380	209752
Biosynthesis of Glucocerebroside 2					Levery et al. (2000), Kanehisa et al. (2002)	ANEW			
r853	:	C191SPH + C181COA ⇒ CEREB2 + COA	2.3.1.24	Ceramide synthase	Levery et al. (2000, Inferred)	ANEW		An11g00990	52868
r854	:	UDPG + CEREB2 ⇒ UDP + GLUCER2	2.4.1.80	2-hydroxyacylsphingosine 1-beta-glucosyltransferase	Levery et al. (2000, Inferred)	ANEW		An07g03380	209752
Biosynthesis of ceramide-P-inositol and trigalactosyldimannosylinositolphosphorylceramide (GPSL G)					Byrne and Brennan (1976), Kanehisa et al. (2002)	ANEW			
r855	:	CERB2 + PINS ⇒ IPC + H_2O	2.-.-.-	IPC synthase, mannosyl diphosphorylinositol ceramide synthase	Zhong et al. (2000)	ANID			
r856	:	IPC + GDPMAN ⇒ MIPC + GDP	SUR1	MIPC synthase	Byrne and Brennan (1976, Inferred)	ANID	*	An05g02310; An09g00100; An15g00630	189424; 43578; 210021
r857	:	MIPC + GDPMAN ⇒ DMIPC + GDP	SUR1	MIPC synthase	Byrne and Brennan (1976, Inferred)	ANID	*	An05g02310; An09g00100; An15g00630	189424; 43578; 210021
r858	:	UDPGAL + DMIPC ⇒ GDMIPC + UDP	2.4.1.-	Galactosyltransferase	Byrne and Brennan (1976, Inferred)	ANEW		An01g09810	170454
r859	:	UDPGAL + GDMIPC ⇒ DGDMIPC + UDP	2.4.1.-	Galactosyltransferase	Byrne and Brennan (1976, Inferred)	ANEW		An01g09810	170454
r860	:	UDPGAL + DGDMIPC ⇒ TGDMIPC + UDP	2.4.1.-	Galactosyltransferase	Byrne and Brennan (1976, Inferred)	ANEW		An01g09810	170454
BIOSYNTHESIS OF LANOSTEROL					Servouse and Karst (1986), Kanehisa et al. (2002), Nemec and Jernejc (2002)	ANIG, ANID			
r861	:	ACCOA + AACCOA + H_2O ⇆ H3MCOA + COA	2.3.3.10	3-hydroxy-3-methylglutaryl coenzyme A synthase		ANID		An02g06320; An07g04260	55566; 56215
r862	:	H3MCOA + 2 NADPH ⇆ MVL + COA + 2 NADP	1.1.1.34	3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase isozyme	Evans and Gealt (1988, A. nidulans)	ANID		An04g00610; An07g08280; An09g03240; An13g04000	213343; 209439; 188317; 44946
r863	:	ATP + MVL ⇒ ADP + PMVL	2.7.1.36	Mevalonate kinase	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID		An04g02190	213169
r864	:	ATP + PMVL ⇒ ADP + PPMVL	2.7.4.2	Phosphomevalonate kinase	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID		An14g04010	211137
r865	:	ATP + PPMVL ⇒ ADP + PI + IPPP + CO_2	4.1.1.33	Diphosphomevalonate decarboxylase	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID		An04g01540	203692
r866	:	IPPP ⇆ DMPP	5.3.3.2	Isopentenyl diphosphate:dimethylallyl diphosphate isomerase (IPP isomerase)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID		An08g07570	52621
r867	:	DMPP + IPPP ⇒ GPP + PPI	2.5.1.1	Prenyltransferase	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID		An11g02500	38877
r868	:	GPP + IPPP ⇒ FPP + PPI	2.5.1.10	Farnesyl diphosphate synthetase (FPP synthetase)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID		An16g01670; An04g04640	125382; 134931
r869	:	2 FPP + NADPH ⇒ NADP + SQL + 2 PPI	2.5.1.21	Squalene synthase	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID		An02g11000	130900
r870	:	SQL + O_2 + NADPH ⇒ S23E + NADP + H_2O	1.14.99.7	Squalene monooxygenase	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANEW		An03g03770	213441
r871	:	S23E ⇒ LNST	5.4.99.7	2,3-oxidosqualene-lanosterol cyclase	Nemec and Jernejc (2002, Inferred), Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID		An07g06150; An09g01330	181224; 189003
BIOSYNTHESIS OF ZYMOSTEROL AND ERGOSTEROL					Servouse and Karst (1986), Kanehisa et al. (2002), Cherry et al. (1998)				
r872	:	LNST + 3 NADPH + 3 O_2 ⇒ DCTOL + FOR + 3 NADP + 4 H_2O	ERG11	Cytochrome p450 lanosterol 14A-demethylase (ERG11)	van den Brink et al. (1996)	ANID		An11g00270; An11g02230	38711; 55947

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r873	:	DCTOL + NADPH ⇒ DCDOL + NADP	ERG24	C-14 sterol reductase (ERG24)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID	An01g07000	51895
r874	:	DCDOL + 3 O_2 + 3 NADPH ⇒ DCDA + 3 NADP + 4 H_2O	ERG25	C-4 sterol methyl oxidase (ERG25)	Chopra and Khuller (1984, Inferred), Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANEW	An03g06410	44595
r875	:	DCDA ⇒ CDOL + CO_2	ERG26	C-4 sterol decarboxylase (ERG26)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANEW	An15g03090	200652
r876	:	CDOL + 3 O_2 + 3 NADPH ⇒ CDA + 3 NADP + 4 H_2O	ERG25	C-4 sterol methyl oxidase (ERG25)	Chopra and Khuller (1984, Inferred), Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANEW	An03g06410	44595
r877	:	CDA ⇒ ZYMST + CO_2	ERG25	C-4 sterol decarboxylase (ERG26)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANEW	An15g03090	200652
r879	:	ZYMST + SAM ⇒ FEST + SAH	2.1.1.41	S-adenosyl-methionine delta-24-sterol-C-methyltransferase (ERG6)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID	An04g04210; An14g01590	213016; 56548
r880	:	FEST ⇆ EPST	ERG2	C-8 sterol isomerase (ERG1)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANID	An01g03350	206219
r881	:	EPST + O_2 + NADPH ⇒ NADP + ERGOD + 2 H_2O	ERG3	C-5 sterol desaturase (ERG3)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANEW	An15g00150; An16g02930	200430; 53645
r882	:	ERGOD + O_2 + NADPH ⇒ NADP + ERGOT + 2 H_2O	ERG5	C-22 sterol desaturase (ERG5)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANEW	An01g02810; An11g03230	206266; 55967
r883	:	ERGOT + NADPH ⇒ ERGOST + NADP	ERG4	C-24 sterol reductase (ERG4)	Ferreira et al. (2005, A. nidulans, A. fumigatus, A. oryzae)	ANEW	An14g05780	49423
METABOLISM OF ERGOSTEROL ESTERS								
r884	:	0.074 C160ACP + 0.222 C181ACP + 0.704 C182ACP + GL3P ⇒ ACP + SEMAGP	2.3.1.15	Glycerol-3-phosphate O-acyltransferase		ANEW	An18g01960	188006
r885	:	0.074 C160ACP + 0.222 C181ACP + 0.704 C182ACP + SEMAGP ⇒ ACP + SEDAGP	2.3.1.51	1-acylglycerol-3-phosphate O-acyltransferase		ANEW	An13g00040	126602
r886	:	SEDAGP + H_2O ⇒ SEDAG + PI	3.1.3.4	phosphatidate phosphatase		ANEW		
r887	:	SEDAG + ERGOST ⇒ SEMAG + ERGOSE	2.3.1.73	sterol O-acyltransferase		ANEW	An18g04660	54192
r888	:	ERGOSE + H_2O ⇒ ERGOST + 0.074 C160 + 0.222 C181 + 0.704 C182	3.1.1.13	sterol esterase		ANEW		
r889	:	SEMAG + H_2O ⇒ 0.074 C160 + 0.222 C181 + 0.704 C182 + GL	3.1.1.23	Acylglycerol lipase		ANEW		
METABOLISM OF COMPLEX LIPIDS					David et al. (2003)	ANIG, ANID		
Glycerolipid biosynthesis					Kanehisa et al. (2002)	ANIG, ANID		
r890	:	0.024 C120ACP + 0.013 C140ACP + 0.012 C141ACP + 0.002 C150ACP + 0.154 C160ACP + 0.02 C161ACP + 0.008 C162ACP + 0.002 C170ACP + 0.026 C180ACP + 0.374 C181ACP + 0.327 C182ACP + 0.032 C183ACP + 0.006 C200ACP + GL3P ⇒ ACP + MAGLYP	2.3.1.15	Glycerol-3-phosphate O-acyltransferase		ANEW	An18g01960	188006
r956	:	MAGLYP + H_2O ⇒ MAGLY + PI	3.1.3.4	phosphatidate phosphatase		ANEW		
r891	:	0.024 C120ACP + 0.013 C140ACP + 0.012 C141ACP + 0.002 C150ACP + 0.154 C160ACP + 0.02 C161ACP + 0.008 C162ACP + 0.002 C170ACP + 0.026 C180ACP + 0.374 C181ACP + 0.327 C182ACP + 0.032 C183ACP + 0.006 C200ACP + MAGLYP ⇒ ACP + DAGLYP	2.3.1.51	Glycerol-3-phosphate O-acyltransferase		ANEW	An13g00040	126602
r892	:	DAGLYP + H_2O ⇒ DAGLY + PI	3.1.3.4	phosphatidate phosphatase		ANEW		
r893	:	0.024 C120ACP + 0.013 C140ACP + 0.012 C141ACP + 0.002 C150ACP + 0.154 C160ACP + 0.02 C161ACP + 0.008 C162ACP + 0.002 C170ACP + 0.026 C180ACP + 0.374 C181ACP + 0.327 C182ACP + 0.032 C183ACP + 0.006 C200ACP + DAGLY ⇒ TAGLY + ACP	2.3.1.20	1-acylglycerol-3-phosphate acyltransferase	Tomoda et al. (1999)	ANID	An12g03600; An15g03770	186422; 181869
Glycerolipid degradation								
r894	:	TAGLY + H_2O ⇒ DAGLY + 0.024 C120 + 0.013 C140 + 0.012 C141 + 0.002 C150 + 0.154 C160 + 0.02 C161 + 0.008 C162 + 0.002 C170 + 0.026 C180 + 0.374 C181 + 0.327 C182 + 0.032 C183 + 0.006 C200	3.1.1.3	Triacylglycerol lipase	Hannan (1959)	ANID	An13g01880; An03g06560; An03g06630; An06g00350; An07g00440; An07g04200; An09g02180; An09g02270; An09g03760; An09g05120; An12g06560; An13g00480; An14g00860; An16g08870	50877; N/A; 191506; 177254; 53361; 39997; 212664; 189135; 43311; 50087; 185927; 191767; 185301; 193610

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r895	:	DAGLY + H_2O ⇒ MAGLY + 0.024 C120 + 0.013 C140 + 0.012 C141 + 0.002 C150 + 0.154 C160 + 0.02 C161 + 0.008 C162 + 0.002 C170 + 0.026 C180 + 0.374 C181 + 0.327 C182 + 0.032 C183 + 0.006 C200	3.1.1.3	Triacylglycerol lipase	Hannan (1959)	ANID	An13g01880; An03g06560; An03g06630; An06g00350; An07g00440; An07g04200; An09g02180; An09g02270; An09g03760; An09g05120; An12g06560; An13g00480; An14g00860; An16g08870	50877; N/A; 191506; 177254; 53361; 39997; 212664; 189135; 43311; 50087; 185927; 191767; 185301; 193610
Glycolipids metabolism					David et al. (2003)	ANIG, ANID		
Mono- and di-galactosyldiglyceride biosynthesis								
r896	:	DAGLY + UDPGAL ⇆ UDP + MGDG	2.4.1.46	UDPgalactose:1,2-diacylglycerol 3-beta-D-galactosyltransferase		ANID		
r897	:	MGDG + UDPGAL ⇆ UDP + DGDG	2.4.1.184	Galactolipid galactosyltransferase		ANID		
Monoglucosyloxyoctadecenoic acid								
r898	:	C181COA + UDPG + H_2O ⇆ MGC181 + UDP + COA	2.4.1.-	lipid galactosyltransferase		ANEW		
SECONDARY METABOLISM								
Ochratoxin A biosynthesis								
r1010	:	4 ACCOA + 1 MALCOA + 1 PHE ⇒ 5 COA + OTA	No EC	Artificial reaction, chlor left out	Abarca et al. (1994), Varga et al. (2003), O'Callaghan et al. (2003), Samson et al. (2004), Blumenthal (2004)	ANEW	An10g00140	44965
PROTEIN PRODUCTION								
Glucoamylase production								
r1266	:	0.951 ALA + 0.307 ARG + 0.366 ASN + 0.644 ASP + 0.146 CYS + 0.249 GLN + 0.38 GLU + 0.687 GLY + 0.059 HIS + 0.351 ILE + 0.702 LEU + 0.190 LYS + 0.044 MET + 0.322 PHE + 0.322 PRO + 1.272 SER + 1.082 THR + 0.278 TRP + 0.395 TYR + 0.614 VAL + 40.39 ATP ⇒ 40.39 ADP + 40.49 PI + GAMYLe	No EC	Artifical protein synthesis reaction		ANEW		
Alphaamylase production								
r1265	:	0.622 ALA + 0.226 ARG + 0.452 ASN + 0.773 ASP + 0.170 CYS + 0.283 GLN + 0.320 GLU + 0.754 GLY + 0.132 HIS + 0.509 ILE + 0.716 LEU + 0.189 LYS + 0.151 MET + 0.264 PHE + 0.358 PRO + 1.018 SER + 0.716 THR + 0.207 TRP + 0.660 TYR + 0.603 VAL + 39.37 ATP ⇒ 39.37 ADP + 39.37 PI + AAMYLe	No EC	Artifical protein synthesis reaction		ANEW		
Sulfur metabolism								
r899	:	H_2SO_3 + 3 NADPH ⇆ H2S + 3 NADP + 3 H_2O	1.8.1.2	Sulfite reductase	Sieńko and Paszewski (1999, A. nidulans)	ANID	An11g06670	208898
r900	:	SLF + ATP ⇒ PPI + APS	2.7.7.4	ATP sulfurylase	Buxton et al. (1989)	ANID	An11g09790	209058
r901	:	APS + ATP ⇒ ADP + PAPS	2.7.1.25	Adenylylsulfate kinase	Borges-Walmsley et al. (1995), Clarke et al. (1997), Sieńko and Paszewski (1999, A. nidulans)	ANID	An08g02990	208264
r902	:	PAPS + RTHIO ⇒ OTHIO + H_2SO_3 + PAP	1.8.4.8	PAPS reductase	Borges-Walmsley et al. (1995), Sieńko and Paszewski (1999, A. nidulans)	ANID	An11g09780	56053
r903	:	CHOSLF + H_2O ⇆ CHO + SLF	3.1.6.6	Choline sulphatase	Scott and Spencer (1968, A. nidulans)	ANEW	An08g08950	55721
r904	:	PAPS + CHO ⇆ PAP + CHOSLF	2.8.2.6	choline sulfotransferase	Hussey and Spencer (1966, A. nidulans)	ANEW		
r905	:	PAP + H_2O ⇒ AMP + PI	3.1.3.7	3′- 5′ bisphosphate nucleotidase		ANID	An11g06820	208912
r112	:	H_2SO_3 ⇆ S + O_2 + H_2O	1.13.11.18	Sulfur dioxygenase	Tepper et al. (1966, Inferred)	ANEW		
Nitrogen metabolism								
r906	:	HNO_3 + NADPH ⇒ HNO_2 + NADP + H_2O	1.7.1.3	Nitrate reductase (niaD)	Unkles et al. (1992)	ANID	An08g05610	208048
r907	:	HNO_2 + 3 NADPH ⇒ NH4OH + 3 NADP + H_2O	1.7.1.4	Nitrite reductase	Unkles et al. (1992)	ANID	An08g05640	198539
r908	:	NH4OH ⇆ NH_3 + H_2O	Non enzymatic step	Non enzymatic reaction		ANEW		
r909	:	UREA + ATP + H_2O + CO_2 ⇆ ADP + PI + UREAC	6.3.4.6	Urea carboxylase		ANID	An01g13810	172796
r910	:	UREAC ⇒ 2 NH_3 + 2 CO_2	3.5.1.54	Allophanate hydrolase		ANID		

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ID		Reaction	EC no	Enzyme	Source	Model		CBS	ATCC
r911	:	ACNL ⇒ INAC + NH_3	3.5.5.1	Nitrilase	Snajdrova et al. (2004)	ANID		An16g00550; An01g07510; An01g12090; An06g01960; An08g08940; An08g10150; An12g01260; An16g06210; An18g01740	41410; 35944; 170270; 175987; N/A; 52578; 141873; 40928; 211815
r912	:	UREA + H_2O ⇒ CO_2 + 2 NH_3	3.5.1.5	urease	Ivanov (1925), Smith et al. (1993)	ANEW		An01g03550; An15g00940	52004; 200521
BIOMASS REACTIONS									
POLYMERIZATION REACTIONS (PROTEINS, DNA, RNA)									
Protein formation									
PROTEIN	:	1.033 ALA + 0.413 ARG + 0.209 ASN + 0.628 ASP + 0.079 CYS + 0.899 GLU + 0.300 GLN + 0.862 GLY + 0.205 HIS + 0.396 ILE + 0.704 LEU + 0.651 LYS + 0.105 MET + 0.312 PHE + 0.441 PRO + 0.628 SER + 0.503 THR + 0.126 TRP + 0.205 TYR + 0.536 VAL + 39.729 ATP + 30.489 H_2O ⇒ 39.729 ADP + 39.729 PI + Protein	Artificial	Artificial reaction		ANEW			
RNA formation									
RNA	:	0.773 AMP + 0.931 GMP + 0.773 CMP + 0.616 UMP + 7.423 ATP + 4.330 H_2O ⇒ 7.424 ADP + 7.424 PI + RNA	2.7.7.6	DNA-directed RNA polymerase		ANEW	*	An01g02200; An01g04380; An01g05740; An01g07250; An01g11950; An01g12710; An02g01800; An02g05460; An02g11470; An08g07050; An09g04100; An11g01770; An11g09370; An12g00720; An12g00780; An12g03900; An13g00280; An15g00700; An15g05780; An15g05790; An16g07430	196819; 36183; 171679; 143936; 205564; 205506; 52135; 206792; 128750; 176941; 128642; 55936; 39394; 54460; 190142; 211641; 57188; 40356; 48809; 48810; 55082
DNA formation									
DNA	:	0.794 DAMP + 0.826 DCMP + 0.794 DTMP + 0.826 DGMP + 11.019 ATP + 7.778 H_2O ⇒ 11.019 ADP + 11.019 PI + DNA	2.7.7.7	DNA-directed DNA polymerase		ANEW	*	An02g02510; An02g14830; An04g02280; An08g02440; An11g00720; An11g09550; An14g06200; An14g06560; An15g07150; An16g03060	206569; 173303; 213157; 176678; 179102; 179788; 184522; 185612; 210383; 53636
Cell wall composition									
Cellwall	:	0.043 GAG + 0.254 NIG + 0.337 PSNIG + 0.381 GGM + 0.389 14GLUCAN + 2.726 13GLUCAN + 1.623 CHIT ⇒ CELLWALL	Artificial	Artificial reaction		ANEW			
Lipids:									
Lipidsassemb	:	0.010083 TAGLY + 0.001009 DAGLY + 0.008912 MAGLY + 0.000223 C140 + 0.001480 C160 + 0.000245 C180 + 0.001678 C181 + 0.001664 C182 + 0.000047 C183 + 0.034062 ERGOST + 0.010038 ERGOSE + 0.030053 MGDG + 0.012374 MGC181 + 0.007859 DGDG + 0.000005 TGDMIPC + 0.000030 CERB1 + 0.000031 CERB2 + 0.000025 GALCER + 0.000024 GLUCER1 + 0.000024 GLUCER2 + 0.001746 CL + 0.015312 PC + 0.000359 PS + 0.034807 PE ⇒ LIPIDS	Artificial	Artificial reaction		ANEW			

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
Small molecules pool:								
Pool	:	0.00039 ICIT + 0.013 CIT + 0.00091 SUCC + 0.00007 FUM + 0.00065 MAL + 0.0017 NAD + 0.00018 NADH + 0.00014 NADP + 0.00008 NADPH + 0.04 TRE + 0.18 MNT + 0.46 GL + 0.3 EOL + 0.01 AOL $\Rightarrow$ POOL	Artificial	Artificial reaction		ANEW		
Biomass formation								
GROWTH	:	0.263 Protein + 0.00244 DNA + 0.01814 RNA + LIPIDS + POOL + 0.38 CELLWALL + 61 ATP + 61 H_2O $\Rightarrow$ 61 ADP + 61 PI + BIOMASS	Artificial	Artificial reaction		ANEW		
Maintenance requirements (non-growth associated)								
m_ATP	:	ATP + H_2O $\Rightarrow$ ADP + PI	Artificial	Artificial reaction		ANIG, ANID		
TRANSPORT PROCESSES								
Non-carrier-mediated (free diffusion)								
Across the cytoplasmastic membrane								
Others:								
r1092	:	CO_2e $\leftrightarrows$ CO_2			David et al. (2003)	ANIG, ANID		
r1093	:	H_2Oe $\leftrightarrows$ H_2O			David et al. (2003)	ANIG, ANID		
r1094	:	O_2e $\Rightarrow$ O_2			David et al. (2003)	ANIG, ANID		
r1091	:	H_2O_2e $\leftrightarrows$ H_2O_2			Pel et al. (2007)	ANEW		
Alcohols:								
r1071	:	ETHe $\leftrightarrows$ ETH			David et al. (2003)	ANIG, ANID		
r1141	:	METHOLe $\leftrightarrows$ METHOL			David et al. (2003)	ANIG, ANID		
Acids:								
r1069	:	ACe $\leftrightarrows$ AC			David et al. (2003)	ANIG, ANID		
r1142	:	FORe $\leftrightarrows$ FOR			Hauge (1957, Inferred)	ANID		
r1066	:	LACe $\leftrightarrows$ LAC			Netik et al. (1997)	ANIG, ANID		
r1065	:	LLACe $\leftrightarrows$ LLAC			Netik et al. (1997)	ANIG, ANID		
Across the mitochondrial membrane								
Others:								
r1150	:	H_2O $\leftrightarrows$ H_2Om			David et al. (2003)	ANIG, ANID		
r1153	:	O_2 $\leftrightarrows$ O_2m			David et al. (2003)	ANIG, ANID		
r1152	:	CO_2 $\leftrightarrows$ CO_2m			David et al. (2003)	ANIG, ANID		
r1151	:	NH_3 $\leftrightarrows$ NH_3m			David et al. (2003)	ANIG, ANID		
Alcohols:								
r1149	:	ETH $\leftrightarrows$ ETHm				ANID		
Aldehydes:								
r1148	:	ACAL $\leftrightarrows$ ACALm				ANID		
Acids:								
r1147	:	AC $\leftrightarrows$ ACm			David et al. (2003)	ANIG, ANID		
Fatty acids:								
r1014	:	C40e $\leftrightarrows$ C40			Chattopadhyay et al. (1985b)	ANEW		
r1015	:	C60e $\leftrightarrows$ C60			Chattopadhyay et al. (1985b)	ANEW		
r1016	:	C80e $\leftrightarrows$ C80			Chattopadhyay et al. (1985b)	ANEW		
r1017	:	C100e $\leftrightarrows$ C100			Chattopadhyay et al. (1985b)	ANEW		
r1018	:	C120e $\leftrightarrows$ C120			Chattopadhyay et al. (1985b)	ANEW		
r1019	:	C140e $\leftrightarrows$ C140			Chattopadhyay et al. (1985b)	ANEW		
r1020	:	C141e $\leftrightarrows$ C141			Chattopadhyay et al. (1985b)	ANEW		
r1021	:	C150e $\leftrightarrows$ C150			Chattopadhyay et al. (1985b)	ANEW		
r1022	:	C160e $\leftrightarrows$ C160			Chattopadhyay et al. (1985b)	ANEW		
r1023	:	C161e $\leftrightarrows$ C161			Chattopadhyay et al. (1985b)	ANEW		
r1024	:	C162e $\leftrightarrows$ C162			Chattopadhyay et al. (1985b)	ANEW		
r1025	:	C170e $\leftrightarrows$ C170			Chattopadhyay et al. (1985b)	ANEW		
r1026	:	C171e $\leftrightarrows$ C171			Chattopadhyay et al. (1985b)	ANEW		

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r1027	:	C180e ⇆ C180			Chattopadhyay et al. (1985b)	ANEW		
r1028	:	C181e ⇆ C181			Chattopadhyay et al. (1985b)	ANEW		
r1029	:	C182e ⇆ C182			Chattopadhyay et al. (1985b)	ANEW		
r1030	:	C183e ⇆ C183			Chattopadhyay et al. (1985b)	ANEW		
r1031	:	C190e ⇆ C190			Chattopadhyay et al. (1985b)	ANEW		
r1032	:	C191e ⇆ C191			Chattopadhyay et al. (1985b)	ANEW		
r1033	:	C192e ⇆ C192			Chattopadhyay et al. (1985b)	ANEW		
r1034	:	C200e ⇆ C200			Chattopadhyay et al. (1985b)	ANEW		
Carrier-mediated								
Across the cytoplasmatic membrane								
Nucleotide related								
r1124	:	ATPe ⇆ ATP		ATP permease	Chowdhury et al. (1997)	ANEW		
r1123	:	AMPe ⇆ AMP		AMP permease	Inferred	ANEW		
r1125	:	ATNe ⇆ ATN		Allantoin permease	Arst and Cove (1969), Martinelli and Kinghorn (1994, A. nidulans)	ANEW		
r1119	:	HYXNe ⇆ HYXN		Hypoxanthine permease	Arst and Cove (1969), Martinelli and Kinghorn (1994, A. nidulans)	ANEW		
r1120	:	URAe ⇆ URAe		Uracil permease	Experimental	ANEW		
r1121	:	URIe ⇆ URIe		Uridine permease	Experimental	ANEW		
r1180	:	ADe ⇆ AD		adenine permease	Martinelli and Kinghorn (1994, A. nidulans)	ANEW		
r1129	:	QUINe ⇆ QUIN		Quinolinate permease		ANEW		
r1126	:	NICAe ⇆ NICA		Nicotinate permease		ANEW		
r1127	:	NICDe ⇆ NICD		Nicotinamide permease		ANEW		
r1122	:	XANe ⇆ XAN		Xanthine permease	Taha and Sharabash (1956, Inferred), Martinelli and Kinghorn (1994, A. nidulans)	ANEW		
r1128	:	KYNe ⇆ KYN		L-Kynurenine permease		ANEW		
r1214	:	3CPYRDe ⇆ 3CPYRD			Snajdrova et al. (2004, Inferred)	ANEW		
Aromatics and catabolic products								
r1182	:	ANe ⇆ AN		Anthranilate transporter	Kamath et al. (1987, Inferred)	ANEW		
r1074	:	PHACe ⇆ PHAC		Phenylacetate transporter	Sugumaran et al. (1973, Inferred)	ANEW		
r1076	:	DMANDe ⇆ DMAND		Mandelate-transporter	Jamaluddin et al. (1970, Inferred)	ANEW		
r1075	:	LMANDe ⇆ LMAND		Mandelate-transporter	Jamaluddin et al. (1970, Inferred)	ANEW		
r1073	:	PHALe ⇆ PHAL				ANEW		
r1078	:	BAe ⇆ BA		benzoate transporter	Martinelli and Kinghorn (1994, Inferred)	ANEW		
r1077	:	BNe ⇆ BN				ANEW		
r1084	:	DHSKe ⇆ DHSK				ANEW		
r1082	:	SALIe ⇆ SALI		salicylate transporter	Krupka et al. (1967), Martinelli and Kinghorn (1994, Inferred)	ANEW		
r1072	:	PHPYRe ⇆ PHPYR				ANEW		
r1079	:	BAMNe ⇆ BAMN				ANEW		
r1083	:	RESe ⇆ RES				ANEW		
r1272	:	COUMe ⇆ COUM			Milstein et al. (1988, Inferred)	ANEW		
r1197	:	DMTe ⇆ DMT			Ganji et al. (1995, Inferred)	ANEW		
r1198	:	TPHTHe ⇆ TPHTH			Ganji et al. (1995, Inferred)	ANEW		
r1199	:	PCCe ⇆ PCC			Ganji et al. (1995, Inferred)	ANEW		
r1204	:	FERe ⇆ FER				ANEW		
r1205	:	VANe ⇆ VAN				ANEW		
r1209	:	INDe ⇆ IND			Kamath and Vaidyanathan (1990, Inferred)	ANEW		
r1212	:	3HBAe ⇆ 3HBA				ANEW		
Alkylamines								
r1190	:	BUTN ⇆ BUTNe				ANEW		
r1223	:	PENN ⇆ PENNe				ANEW		
Others								
r1095	:	PIe ⇆ PI			Seshadri et al. (2004, Inferred)	ANIG, ANID		
r1087	:	NH_3e ⇆ NH_3			David et al. (2003)	ANEW		
r1086	:	HNO_3e ⇆ HNO_3			Seshadri et al. (2004, Inferred)	ANEW		
r1088	:	H_2SO_3e ⇒ H_2SO_3				ANID		
r1089	:	CHOSLFe ⇆ CHOSLF		Choline sulphate permease	Scott and Spencer (1968, A. nidulans)	ANEW		
r1090	:	SLFe ⇆ SLF		Sulphate permease	Marzluf (1993), Borges-Walmsley et al. (1995, A. nidulans)	ANIG		
r1118	:	DTBe ⇆ DTB			Parry and Naidu (1980, Inferred)	ANEW		
r1085	:	UREAe ⇆ UREA			Ivanov (1925)	ANEW		
r1012	:	OTA ⇒ OTAe		Ochratoxin A exporter		ANEW		
r1273	:	GLYNe ⇆ GLYN			Witteveen et al. (1990a, Inferred)	ANEW		
CARBOHYDRATES								
Dissacharides								

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r1143	:	TREe ⇆ TRE				ANID		
r1144	:	LACTe ⇒ LACT				ANIG, ANID		
r1145	:	MLTe ⇒ MLT			Pendl et al. (2004)	ANIG, ANID		
Monosacharides								
Hexoses								
r1037	:	GLACe ⇒ GLAC			vanKuyk et al. (2004)	ANIG, ANID		
r1047	:	GLCe ⇒ GLC			Karaffa et al. (2001)	ANIG, ANID		
r1048	:	DGLCe ⇆ DGLC				ANIG		
r1046	:	bDGLCe ⇒ bDGLC			David et al. (2003)	ANIG, ANID		
r1044	:	FRUe ⇒ FRU			Karaffa et al. (2001), vanKuyk et al. (2004)	ANIG, ANID		
r1041	:	MANe ⇒ MAN			vanKuyk et al. (2004)	ANIG, ANID		
r1039	:	IDOLe ⇆ IDOL				ANIG, ANID		
r1040	:	SORe ⇆ SOR			Seshadri et al. (2004, Inferred)	ANIG, ANID		
r1221	:	RHAe ⇆ RHA			Fries and Kallstromer (1965, Inferred)	ANEW		
Pentoses								
r1052	:	ARABe ⇒ ARAB			David et al. (2003)	ANIG, ANID		
r1059	:	LARABe ⇒ LARAB			de Groot et al. (2003)	ANIG, ANID		
r1049	:	RIBe ⇒ RIB			David et al. (2003)	ANIG, ANID		
r1051	:	RLe ⇒ RL				ANID		
r1054	:	XYLe ⇒ XYL			Martinelli and Kinghorn (1994), Prathumpai et al. (2003), de Groot et al. (2003), vanKuyk et al. (2004)	ANIG, ANID		
r1055	:	XULe ⇒ XUL				ANID		
r1056	:	LXULe ⇒ LXUL				ANID		
Tetroses								
r1062	:	Ee ⇒ E			Schuurink et al. (1990)	ANID		
r1060	:	EUe ⇒ EU				ANID		
ALCOHOLS (polyols)								
r1064	:	GLe ⇆ GL			Martinelli and Kinghorn (1994)	ANIG, ANID		
r1061	:	EOLe ⇆ EOL			David et al. (2003)	ANIG, ANID		
r1053	:	AOLe ⇆ AOL			Martinelli and Kinghorn (1994)	ANIG, ANID		
r1058	:	LAOLe ⇆ LAOL			Martinelli and Kinghorn (1994)	ANIG, ANID		
r1050	:	RIBOLe ⇆ RIBOL			David et al. (2003)	ANIG, ANID		
r1057	:	XOLe ⇆ XOL			Prathumpai et al. (2003)	ANIG, ANID		
r1038	:	GALOLe ⇆ GALOL				ANID		
r1043	:	MNTe ⇆ MNT			Martinelli and Kinghorn (1994)	ANIG, ANID		
r1042	:	SOTe ⇆ SOT			Martinelli and Kinghorn (1994)	ANIG, ANID		
ACIDS								
TCA cycle related organic acids								
r1139	:	MALe ⇆ MAL			Netik et al. (1997), Alvarez-Vasquez et al. (2000)	ANIG, ANID		
r1138	:	AKGe ⇆ AKG			Netik et al. (1997)	ANIG, ANID		
r1137	:	ACOe ⇆ ACO				ANID		
r1134	:	CITe ⇆ CIT			Burgstaller (2006), Netik et al. (1997)	ANIG, ANID		
r1136	:	FUMe ⇆ FUM			David et al. (2003)	ANIG, ANID		

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r1135	:	ICITe ⇆ ICIT			Netik et al. (1997)	ANID		
r1140	:	OXALe ⇆ OXAL			David et al. (2003)	ANIG, ANID		
r1132	:	OAe ⇆ OA				ANID		
r1131	:	PYRe ⇆ PYR			Netik et al. (1997), Alvarez-Vasquez et al. (2000)	ANIG, ANID		
r1130	:	SUCCe ⇆ SUCC			Netik et al. (1997)	ANIG, ANID		
Other acids								
r1036	:	GALNTe ⇆ GALNT				ANID		
r1035	:	GALUNTe ⇒ GALUNT			Martinelli and Kinghorn (1994)	ANIG, ANID		
r1045	:	GLCNTe ⇆ GLCNT			Muller (1986, Inferred)	ANIG, ANID		
r1179	:	GLCUNTe ⇆ GLCUNT			David et al. (2003)	ANIG, ANID		
r1178	:	KOJAe ⇆ KOJA				ANID		
r1063	:	TARe ⇆ TAR			Patil and Ramakrishnan (1966)	ANIG, ANID		
r1067	:	PROPe ⇆ PROP			Sealy-Lewis and Fairhurst (1998, Inferred)	ANIG, ANID		
r1096	:	QTe ⇆ QT			Cain (1972a, Inferred)	ANEW		
r1097	:	SMEe ⇆ SME			Cain (1972a, Inferred)	ANEW		
r1185	:	GABAe ⇆ GABA			Kumar and Punekar (1998, Inferred)	ANEW	An16g02000	210724
AMINO ACIDS								
r1098	:	GLYe ⇒ GLY				ANID		
r1099	:	ALAe ⇒ ALA			Oganesyan et al. (1998, Inferred)	ANID		
r1100	:	bALAe ⇒ bALA			Sarma et al. (1961, Inferred)	ANID		
r1101	:	ARGe ⇒ ARG				ANID		
r1102	:	ASNe ⇒ ASN				ANID		
r1103	:	ASPe ⇒ ASP			Sarma et al. (1961, Inferred)	ANID		
r1104	:	CYSe ⇒ CYS				ANID		
r1105	:	GLUe ⇒ GLU				ANID		
r1106	:	GLNe ⇒ GLN			Ram et al. (2004, Inferred)	ANID		
r1107	:	HISe ⇒ HIS				ANID		
r1108	:	ILEe ⇒ ILE				ANID		
r1109	:	LEUe ⇒ LEU				ANID		
r1110	:	LYSe ⇒ LYS				ANID		
r1111	:	METe ⇒ MET				ANID		
r1112	:	PHEe ⇒ PHE				ANID		
r1113	:	PROe ⇒ PRO			Jones et al. (1981, A. nidulans)	ANID		
r1114	:	SERe ⇒ SER				ANID		
r1115	:	THRe ⇒ THR				ANID		
r1080	:	TRPe ⇒ TRP			Sarma et al. (1961, Inferred)	ANID		
r1116	:	TYRe ⇒ TYR				ANID		
r1117	:	VALe ⇒ VAL				ANID		
r1184	:	CITRe ⇆ CITR			Lenouvel et al. (2002, Inferred)	ANEW		
r1187	:	ORNe ⇆ ORN			Lenouvel et al. (2002, Inferred)	ANEW		
ALDEHYDES								
r1068	:	PROPALe ⇒ PROPAL			Kazimirova and Novotelnov (1956, Inferred)	ANEW		
r1070	:	ACALe ⇆ ACAL			Rippel and Wiangke (1941, Inferred)	ANEW		
Across the mitochondrial membrane								
OTHERS								
r1154	:	PIm ⇆ PI		Phosphate carrier		ANIG, ANID		
r1181	:	UREA ⇆ UREAm				ANEW		
ACIDS								
r1146	:	PYR ⇒ PYRm			Karaffa et al. (2001), Karaffa and Kubicek (2003)	ANIG, ANID		
r1169	:	CITm + MAL ⇒ CIT + MALm			Karaffa et al. (2001), Karaffa and Kubicek (2003), Pel et al. (2007)	ANIG, ANID	An11g11230; An18g00070	136079; 42578
r1170	:	ACOm + MAL ⇒ ACO + MALm				ANID		
r1171	:	ICITm + MAL ⇒ ICIT + MALm			David et al. (2003)	ANIG, ANID		
r1172	:	AKG ⇆ AKGm				ANID		
r1173	:	OA ⇆ OAm			Karaffa et al. (2001), Pel et al. (2007)	ANID	An14g06860	41991
r1174	:	SUCC ⇆ SUCCm			David et al. (2003)	ANIG, ANID		

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ID		Reaction	EC no	Enzyme	Source	Model	CBS	ATCC
r1175	:	FUM ⇆ FUMm				ANID		
r1176	:	ICIT ⇆ ICITm				ANIG, ANID		
r1168	:	FOR ⇆ FORm			Cossins and Chen (1997, Inferred)	ANEW		
r1166	:	THF ⇆ THFm			Cossins and Chen (1997, Inferred)	ANEW		
r1167	:	METHF ⇆ METHFm			Cossins and Chen (1997, Inferred)	ANEW		
r1177	:	CAP ⇆ CAPm				ANEW		
r1155	:	3OA ⇆ 3OAm				ANEW		
r1186	:	GABA ⇆ GABAm			Kumar and Punekar (1998, Inferred)	ANEW		
r1133	:	GLX ⇆ GLXm				ANEW		
r1191	:	PROPm ⇆ PROP				ANEW		
AMINO ACIDS								
r1158	:	THRm ⇆ THR				ANEW		
r1159	:	ARGm ⇆ ARG				ANEW		
r1160	:	ASPm ⇆ ASP				ANEW		
r1161	:	LEUm ⇆ LEU				ANEW		
r1162	:	ILEm ⇆ ILE				ANEW		
r1163	:	ORNm ⇆ ORN				ANEW		
r1164	:	VALm ⇆ VAL				ANEW		
r1165	:	LYSm ⇆ LYS				ANEW		
r1183	:	CITR ⇆ CITRm			Lenouvel et al. (2002, Inferred)	ANEW		
Shuttles								
Malate-Aspartate shuttle								
r1157	:	ASPm + GLU ⇆ ASP + GLUm			David et al. (2003)	ANIG, ANID		
r1156	:	MAL + AKGm ⇆ MALm + AKG				ANID		

Table A.2: List of the abbreviations for metabolite-names used in the reaction list of *A. niger iMA871 (App A.1) and their full name. An "m" denotes that the metabolite is found in the mitochondrion, whereas an "e" is used to mark an extracellular metabolite.*

Abbreviation	Full name
13GLUCAN	1,3-beta-D-Glucan
13GLUCANe	1,3-beta-D-Glucan (extracellular)
13PDG	1,3-Bisphospho-D-glycerate
14GLUCAN	1,4-alphaglucan
2D3DGALT	2-Dehydro-3-deoxy-D-galactonate
2HPAC	2-hydroxyphenylacetic acid
2MAC	2-maleyl acetate
2MACOm	2-methyl aconitate
2MCITm	2-methyl citrate
2MICITm	2-methyl isocitrate
2PG	2-Phospho-D-glycerate
345THBe	Gallic acid
3CMUCO	3-Carboxymuconate
3CPYRD	3-cyanopyridine
3CPYRDe	3-cyanopyridine (extracellular)
3DDAH7P	2-Dehydro-3-deoxy-D-arabino-heptonate 7-phosphate
3FPYR	3-fumarylpyruvate
3HBA	3-hydroxybenzoate; m-hydroxybenzoate
3HBAe	3-hydroxybenzoate; m-hydroxybenzoate (extracellular)
3HIND	3-hydroxyindoxyle
3HPYR	3-hydroxypyruvate
3MPYR	3-maleylpyruvate
3OA	3-oxoadipate
3OACOAm	3-oxoadipyl-CoA
3OAm	3-oxoadipate
3PG	3-Phospho-D-glycerate
3PSER	3-Phosphoserine
3PSME	5-O-(1-Carboxyvinyl)-3-phosphoshikimate
4CMUCL	4-Carboxymuconolactone
4HBA	4-hydroxybenzoic acid
4HBAL	4-hydroxybenzaldehyde
4HBFOR	4-hydroxybenzoylformic acid
4HMAND	4-hydroxymandelate
4HPAC	4-hydroxyphenylacetic acid
4HPP	3-(4-Hydroxyphenyl)pyruvate
4PPNCYS	(R)-4’-Phosphopantothenoyl-L-cysteine
4PPNTE	Pantetheine 4’-phosphate
4PPNTO	D-4’-Phosphopantothenate
AACACP	Acetoacetyl [acyl-carrier protein]
AACCOA	Acetoacetyl coenzyme A
AACCOAm	Acetoacetyl coenzyme A (mitochondrial)
AAMYLe	Alpha-amylase (secreted to the medium)

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Abbreviation	Full name
ABUTm	2-Aceto-2-hydroxy butyrate (mitochondrial)
AC	Acetate
ACACP	Acyl-[acyl-carrier protein]
ACAL	Acetaldehyde
ACALe	Acetaldehyde, extracellular
ACALm	Acetaldehyde (mitochondrial)
ACCOA	Acetyl coenzyme A
ACCOAm	Acetyl coenzyme A (mitochondrial)
ACe	Acetate (extracellular)
ACLACm	2-Acetolactate (mitochondrial)
ACm	Acetate (mitochondrial)
ACNL	3-Indoleacetonitrile
ACO	cis-Aconitate
ACOe	cis-Aconitate (extracellular)
ACOm	cis-Aconitate (mitochondrial)
ACP	Acyl-carrier protein
ACTAC	Acetoacetate
ACTP	Acetyl phosphate
ACYBUT	gamma-Amino-gamma-cyanobutanoate
AD	Adenine
ADCHOR	4-Amino-4-deoxychorismate
ADe	Adenine (extracellular)
ADHLIPOm	S-Acetyldihydrolipoamide (mitochondrial)
ADN	Adenosine
ADP	ADP
ADPm	ADP (mitochondrial)
ADPR	ADP-Ribose
AHHMD	2-Amino-7,8-dihydro-4-hydroxy-6-(diphosphooxymethyl)pteridine
AHHMP	2-Amino-4-hydroxy-6-hydroxymethyl-7,8-dihydropteridine
AHTD	2-Amino-4-hydroxy-6-(erythro-1,2,3-trihydroxypropyl)-dihydropteridine triphosphate
AICAR	AICAR
AIR	Aminoimidazole ribotide
AKAm	2-Oxoadipate (mitochondrial)
AKG	2-Oxoglutarate
AKGe	2-Oxoglutarate (extracellular)
AKGE1m	α-ketoglutarate bound to α-ketoglutarate dehydrogenase
AKGE2m	α-ketoglutarate bound to dihydrolipoyl transsuccinylase
AKGm	2-Oxoglutarate (mitochondrial)
AKP	2-Dehydropantoate
ALA	L-Alanine
ALAe	L-Alanine (extracellular)
ALAm	L-Alanine (mitochondrial)
AMAm	2-aminoadipate (mitochondrial)
AMASAm	2-aminoadipate-semialdehyde (mitochondrial)
AMP	AMP

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Abbreviation	Full name
AMPe	AMP, extracellular
AMPm	AMP (mitochondrial)
AMYLPe	Amylopectin (extracellular)
AMYLSe	Amylose (extracellular)
AN	Anthranilate
ANe	Anthranilate (extracellular)
AOL	D-Arabitol
AOLe	D-Arabitol (extracellular)
AONA	8-Amino-7-oxononanoate
APROP	α-Aminopropiononitrile
APS	Adenylylsulfate
ARAB	D-Arabinose
ARABe	D-Arabinose (extracellular)
ARABINe	Arabinan (extracellular)
ARABLAC	D-Arabinono-1,4-lactone
ARG	L-Arginine
ARGe	L-Arginine (extracellular)
ARGm	L-Arginine (mitchondrial)
ARGSUCCm	Argininosuccinate (mitchondrial)
ASER	O-Acetyl-L-serine
ASN	L-Asparagine
ASNe	L-Asparagine (extracellular)
ASP	L-Aspartate
ASPe	L-Aspartate (extracellular)
ASPm	L-Aspartate (mitochondrial)
ASPSA	L-Aspartate 4-semialdehyde
ASUC	N6-(1,2-Dicarboxyethyl)-AMP
ATN	Allantoin
ATNe	Allantoin (extracellular)
ATP	ATP
ATPe	ATP (extracellular)
ATPm	ATP (mitochondrial)
ATT	Allantoate
BA	Benzoic acid
BAe	Benzoic acid (extracellular)
BAL	Benzaldehyde
bALA	β-Alanine
bALAe	β-Alanine (extracellular)
BAMN	Benzoylamine
BAMNe	Benzoylamine (extracellular)
BASP	4-Phospho-L-aspartate
BCCP	Biotin-carboxyl-carrier protein
bDG6P	β-D-Glucose 6-phosphate
bDGLC	β-D-Glucose
bDGLCe	β-D-Glucose (extracellular)
BFOR	Benzoylformate

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Abbreviation	Full name
bFRU	β-D-fructose
bGLAC	β-D-galactose
bLARAB	β-L-arabinose
BN	Benzonitrile
BNe	Benzonitrile (extracellular)
BT	Biotin
BTe	Biotin (extracellular)
BTOL	benzene-1,2,4-triol
BUTAL	Butanal
BUTN	n-butylamine
BUTNe	n-butylamine (extracellular)
C100	Decanoate
C100ACP	Decanoyl-[acyl-carrier protein]
C100COA	Decanoyl-CoA
C100COAm	Decanoyl-CoA (mitochondrial)
C100e	Decanoate (extracellular)
C10DACP	Dec-2-enoyl-[acyl-carrier protein]
C10DCOAm	Dec-2-enoyl-CoA (mitochondrial)
C10HACP	3-hydroxydecanoyl-[acyl-carrier protein]
C10HCOAm	3-hydroxydecanoyl-CoA (mitochondrial)
C10OACP	3-oxodecanoyl-[acyl-carrier protein]
C10OCOAm	3-oxodecanoyl-CoA (mitochondrial)
C110ACP	Undecanoyl-[acyl-carrier protein]
C110COAm	Undecanoyl-CoA (mitochondrial)
C11DACP	Undec-2-enoyl-[acyl-carrier protein]
C11DCOAm	Undec-2-enoyl-CoA (mitochondrial)
C11HACP	3-hydroxyundecanoyl-[acyl-carrier protein]
C11HCOAm	3-hydroxyundecanoyl-CoA (mitochondrial)
C11OACP	3-oxoundecanoyl-[acyl-carrier protein]
C11OCOAm	3-oxoundecanoyl-CoA (mitochondrial)
C120	Dodecanoate
C120ACP	Dodecanoyl-[acyl-carrier protein]
C120CAR	Dodecanoyl-carnitine
C120CARm	Dodecanoyl-carnitine (mitochondrial)
C120COA	Dodecanoyl-CoA
C120COAm	Dodecanoyl-CoA (mitochondrial)
C120e	Dodecanoate (extracellular)
C12DACP	Dodec-2-enoyl-[acyl-carrier protein]
C12DCOAm	Dodec-2-enoyl-CoA (mitochondrial)
C12HACP	3-hydroxydodecanoyl-[acyl-carrier protein]
C12HCOAm	3-hydroxydodecanoyl-CoA (mitochondrial)
C12OACP	3-oxododecanoyl-[acyl-carrier protein]
C12OCOAm	3-oxododecanoyl-CoA (mitochondrial)
C130ACP	Tridecanoyl-[acyl-carrier protein]
C130COAm	Tridecanoyl-CoA (mitochondrial)
C13DACP	Tridec-2-enoyl-[acyl-carrier protein]

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Abbreviation	Full name
C13DCOAm	Tridec-2-enoyl-CoA (mitochondrial)
C13HACP	3-hydroxytridecanoyl-[acyl-carrier protein]
C13HCOAm	3-hydroxytridecanoyl-CoA (mitochondrial)
C13OACP	3-oxotridecanoyl-[acyl-carrier protein]
C13OCOAm	3-oxotridecanoyl-CoA (mitochondrial)
C140	Tetradecanoate
C140ACP	Tetradecanoyl-[acyl-carrier protein]
C140CAR	Tetradecanoyl-carnitine
C140CARm	Tetradecanoyl-carnitine (mitochondrial)
C140COA	Tetradecanoyl-CoA
C140COAm	Tetradecanoyl-CoA (mitochondrial)
C140e	Tetradecanoate (extracellular)
C141	Tetradecenoate
C141ACP	Tetradecenoyl-[acyl-carrier protein]
C141CAR	Tetradecenoyl-carnitine
C141CARm	Tetradecenoyl-carnitine (mitochondrial)
C141COA	Tetradecenoyl-CoA
C141COAm	Tetradecenoyl-CoA (mitochondrial)
C141e	Tetradecenoate (extracellular)
C14DACP	Tetradec-2-enoyl-[acyl-carrier protein]
C14DCOAm	Tetradec-2-enoyl-CoA (mitochondrial)
C14HACP	3-hydroxytetradecanoyl-[acyl-carrier protein]
C14HCOAm	3-hydroxytetradecanoyl-CoA (mitochondrial)
C14OACP	3-oxotetradecanoyl-[acyl-carrier protein]
C14OCOAm	3-oxotetradecanoyl-CoA (mitochondrial)
C150	Pentadecanoate
C150ACP	Pentadecanoyl-[acyl-carrier protein]
C150CAR	Pentadecanoyl-carnitine
C150CARm	Pentadecanoyl-carnitine (mitochondrial)
C150COA	Pentadecanoyl-CoA
C150COAm	Pentadecanoyl-CoA (mitochondrial)
C150e	Pentadecanoate (extracellular)
C15DACP	Pentadec-2-enoyl-[acyl-carrier protein]
C15DCOAm	Pentadec-2-enoyl-CoA (mitochondrial)
C15HACP	3-hydroxypentadecanoyl-[acyl-carrier protein]
C15HCOAm	3-hydroxypentadecanoyl-CoA (mitochondrial)
C15OACP	3-oxopentadecanoyl-[acyl-carrier protein]
C15OCOAm	3-oxopentadecanoyl-CoA (mitochondrial)
C160	Hexadecanoate
C160ACP	Hexadecanoyl-[acyl-carrier protein]
C160CAR	Hexadecanoyl-carnitine
C160CARm	Hexadecanoyl-carnitine (mitochondrial)
C160COA	Hexadecanoyl-CoA
C160COAm	Hexadecanoyl-CoA (mitochondrial)
C160e	Hexadecanoate (extracellular)
C161	Hexadecenoate

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Abbreviation	Full name
C161ACP	Hexadecenoyl-[acyl-carrier protein]
C161CAR	Hexadecenoyl-carnitine
C161CARm	Hexadecenoyl-carnitine (mitochondrial)
C161COA	Hexadecenoyl-CoA
C161COAm	Hexadecenoyl-CoA (mitochondrial)
C161e	Hexadecenoate (extracellular)
C162	Hexadecadienoate
C162ACP	Hexadecadienoyl-[acyl-carrier protein]
C162CAR	Hexadecadienoyl-carnitine
C162CARm	Hexadecadienoyl-carnitine (mitochondrial)
C162COA	Hexadecadienoyl-CoA
C162COAm	Hexadecadienoyl-CoA (mitochondrial)
C162e	Hexadecadienoate (extracellular)
C16DACP	Hexadec-2-enoyl-[acyl-carrier protein]
C16DCOAm	Hexadec-2-enoyl-CoA (mitochondrial)
C16HACP	3-hydroxyhexadecanoyl-[acyl-carrier protein]
C16HCOAm	3-hydroxyhexadecanoyl-CoA (mitochondrial)
C16OACP	3-oxohexadecanoyl-[acyl-carrier protein]
C16OCOAm	3-oxohexadecanoyl-CoA (mitochondrial)
C170	Heptadecanoate
C170ACP	Heptadecanoyl-[acyl-carrier protein]
C170CAR	Heptadecanoyl-carnitine
C170CARm	Heptadecanoyl-carnitine (mitochondrial)
C170COA	Heptadecanoyl-CoA
C170COAm	Heptadecanoyl-CoA (mitochondrial)
C170e	Heptadecanoate (extracellular)
C171	Heptadecenoate
C171ACP	Heptadecenoyl-[acyl-carrier protein]
C171CAR	Heptadecenoyl-carnitine
C171CARm	Heptadecenoyl-carnitine (mitochondrial)
C171COA	Heptadecenoyl-CoA
C171COAm	Heptadecenoyl-CoA (mitochondrial)
C171e	Heptadecenoate (extracellular)
C17DACP	Heptadec-2-enoyl-[acyl-carrier protein]
C17DCOAm	Heptadec-2-enoyl-CoA (mitochondrial)
C17HACP	3-hydroxyheptadecanoyl-[acyl-carrier protein]
C17HCOAm	3-hydroxyheptadecanoyl-CoA (mitochondrial)
C17OACP	3-oxoheptadecanoyl-[acyl-carrier protein]
C17OCOAm	3-oxoheptadecanoyl-CoA (mitochondrial)
C180	Octadecanoate
C180ACP	Octadecanoyl-[acyl-carrier protein]
C180CAR	Octadecanoyl-carnitine
C180CARm	Octadecanoyl-carnitine (mitochondrial)
C180COA	Octadecanoyl-CoA
C180COAm	Octadecanoyl-CoA (mitochondrial)
C180e	Octadecanoate (extracellular)

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Abbreviation	Full name
C181	Octadecenoate
C181ACP	Octadecenoyl-[acyl-carrier protein]
C181CAR	Octadecenoyl-carnitine
C181CARm	Octadecenoyl-carnitine (mitochondrial)
C181COA	Octadecenoyl-CoA
C181COAm	Octadecenoyl-CoA (mitochondrial)
C181e	Octadecenoate (extracellular)
C182	Octadecadienoate
C182ACP	Octadecadienoyl-[acyl-carrier protein]
C182CAR	Octadecadienoyl-carnitine
C182CARm	Octadecadienoyl-carnitine (mitochondrial)
C182COA	Octadecadienoyl-CoA
C182COAm	Octadecadienoyl-CoA (mitochondrial)
C182e	Octadecadienoate (extracellular)
C183	Octadecatrienoate
C183ACP	Octadecatrienoyl-[acyl-carrier protein]
C183CAR	Octadecatrienoyl-carnitine
C183CARm	Octadecatrienoyl-carnitine (mitochondrial)
C183COA	Octadecatrienoyl-CoA
C183COAm	Octadecatrienoyl-CoA (mitochondrial)
C183e	Octadecatrienoate (extracellular)
C18DACP	Octadec-2-enoyl-[acyl-carrier protein]
C18DCOAm	Octadec-2-enoyl-CoA (mitochondrial)
C18DHSPH	3-dehydrosphinganine(C18)
C18HACP	3-hydroxyoctadecanoyl-[acyl-carrier protein]
C18HCOAm	3-hydroxyoctadecanoyl-CoA (mitochondrial)
C18OACP	3-oxooctadecanoyl-[acyl-carrier protein]
C18OCOAm	3-oxooctadecanoyl-CoA (mitochondrial)
C18PSPH	Phytosphingosine(C18)
C18SPH	Sphinganine(C18)
C190	Nonadecanoate
C190ACP	Nonadecanoyl-[acyl-carrier protein]
C190CAR	Nonadecanoyl-carnitine
C190CARm	Nonadecanoyl-carnitine (mitochondrial)
C190COA	Nonadecanoyl-CoA
C190COAm	Nonadecanoyl-CoA (mitochondrial)
C190e	Nonadecanoate (extracellular)
C191	Nonadecenoate
C191ACP	Nonadecenoyl-[acyl-carrier protein]
C191CAR	Nonadecenoyl-carnitine
C191CARm	Nonadecenoyl-carnitine (mitochondrial)
C191COA	Nonadecenoyl-CoA
C191COAm	Nonadecenoyl-CoA (mitochondrial)
C191DHSPH	3-dehydrosphinganine(C19:1)
C191e	Nonadecenoate (extracellular)
C191SPH	Sphinganine(C19:1)

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Abbreviation	Full name
C192	Nonadecadienoate
C192ACP	Nonadecadienoyl-[acyl-carrier protein]
C192CAR	Nonadecadienoyl-carnitine
C192CARm	Nonadecadienoyl-carnitine (mitochondrial)
C192COA	Nonadecadienoyl-CoA
C192COAm	Nonadecadienoyl-CoA (mitochondrial)
C192e	Nonadecadienoate (extracellular)
C19DACP	Nonadec-2-enoyl-[acyl-carrier protein]
C19DCOAm	Nonadec-2-enoyl-CoA (mitochondrial)
C19HACP	3-hydroxynonadecanoyl-[acyl-carrier protein]
C19HCOAm	3-hydroxynonadecanoyl-CoA (mitochondrial)
C19OACP	3-oxononadecanoyl-[acyl-carrier protein]
C19OCOAm	3-oxononadecanoyl-CoA (mitochondrial)
C200	Eicosanoate
C200ACP	Eicosanoyl-[acyl-carrier protein]
C200CAR	Eicosanoyl-carnitine
C200CARm	Eicosanoyl-carnitine (mitochondrial)
C200COA	Eicosanoyl-CoA
C200COAm	Eicosanoyl-CoA (mitochondrial)
C200e	Eicosanoate (extracellular)
C20DACP	Eicos-2-enoyl-[acyl-carrier protein]
C20DCOAm	Eicos-2-enoyl-CoA (mitochondrial)
C20DHSPH	3-dehydrosphinganine(C20)
C20HACP	3-hydroxyeicosanoyl-[acyl-carrier protein]
C20HCOAm	3-hydroxyeicosanoyl-CoA (mitochondrial)
C20OACP	3-oxoeicosanoyl-[acyl-carrier protein]
C20OCOAm	3-oxoeicosanoyl-CoA (mitochondrial)
C20PSPH	Phytosphingosine(C20)
C20SPH	Sphinganine(C20)
C40	Butanoate
C40ACP	Butanoyl-[acyl-carrier protein]
C40COA	Butanoyl-CoA
C40COAm	Butanoyl-CoA (mitochondrial)
C40e	Butanoate (extracellular)
C4DACP	But-2-enoyl-[acyl-carrier protein]
C4DCOAm	But-2-enoyl-CoA (mitochondrial)
C4HACP	3-hydroxybutanoyl-[acyl-carrier protein]
C4HCOAm	3-hydroxybutanoyl-CoA (mitochondrial)
C50ACP	Pentanoyl-[acyl-carrier protein]
C50COA	Pentanoyl-CoA
C50COAm	Pentanoyl-CoA (mitochondrial)
C5DACP	Pent-2-enoyl-[acyl-carrier protein]
C5DCOAm	Pent-2-enoyl-CoA (mitochondrial)
C5HACP	3-hydroxypentanoyl-[acyl-carrier protein]
C5HCOAm	3-hydroxypentanoyl-CoA (mitochondrial)
C5OACP	3-oxopentanoyl-[acyl-carrier protein]

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Abbreviation	Full name
C5OCOAm	3-oxopentanoyl-CoA (mitochondrial)
C60	Hexanoate
C60ACP	Hexanoyl-[acyl-carrier protein]
C60COA	Hexanoyl-CoA
C60COAm	Hexanoyl-CoA (mitochondrial)
C60e	Hexanoate (extracellular)
C6DACP	Hex-2-enoyl-[acyl-carrier protein]
C6DCOAm	Hex-2-enoyl-CoA (mitochondrial)
C6HACP	3-hydroxyhexanoyl-[acyl-carrier protein]
C6HCOAm	3-hydroxyhexanoyl-CoA (mitochondrial)
C6OACP	3-oxohexanoyl-[acyl-carrier protein]
C6OCOAm	3-oxohexanoyl-CoA (mitochondrial)
C70ACP	Heptanoyl-[acyl-carrier protein]
C70COAm	Heptanoyl-CoA (mitochondrial)
C7DACP	Hept-2-enoyl-[acyl-carrier protein]
C7DCOAm	Hept-2-enoyl-CoA (mitochondrial)
C7HACP	3-hydroxyheptanoyl-[acyl-carrier protein]
C7HCOAm	3-hydroxyheptanoyl-CoA (mitochondrial)
C7OACP	3-oxoheptanoyl-[acyl-carrier protein]
C7OCOAm	3-oxoheptanoyl-CoA (mitochondrial)
C80	Octanoate
C80ACP	Octanoyl-[acyl-carrier protein]
C80COA	Octanoyl-CoA
C80COAm	Octanoyl-CoA (mitochondrial)
C80e	Octanoate (extracellular)
C8DACP	Oct-2-enoyl-[acyl-carrier protein]
C8DCOAm	Oct-2-enoyl-CoA (mitochondrial)
C8HACP	3-hydroxyoctanoyl-[acyl-carrier protein]
C8HCOAm	3-hydroxyoctanoyl-CoA (mitochondrial)
C8OACP	3-oxooctanoyl-[acyl-carrier protein]
C8OCOAm	3-oxooctanoyl-CoA (mitochondrial)
C90ACP	Nonanoyl-[acyl-carrier protein]
C90COAm	Nonanoyl-CoA (mitochondrial)
C9DACP	Non-2-enoyl-[acyl-carrier protein]
C9DCOAm	Non-2-enoyl-CoA (mitochondrial)
C9HACP	3-hydroxynonanoyl-[acyl-carrier protein]
C9HCOAm	3-hydroxynonanoyl-CoA (mitochondrial)
C9OACP	3-oxononanoyl-[acyl-carrier protein]
C9OCOAm	3-oxononanoyl-CoA (mitochondrial)
CAASP	N-Carbamoyl-L-aspartate
CAIR	1-(5-Phospho-D-ribosyl)-5-amino-4-imidazolecarboxylate
CALH	2-(3-Carboxy-3-aminopropyl)-L-histidine
cAMP	3’,5’-Cyclic AMP
cAMPe	3’,5’-Cyclic AMP (extracellular)
CAP	Carbamoyl phosphate
CAPm	Carbamoyl phosphate (Mitochondrial)

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Abbreviation	Full name
CAR	Carnitine
CARm	Carnitine (mitochondrial)
CBCCP	Carboxybiotin-carboxyl-carrier protein
CCL	Catechol
cCMP	3’,5’-Cyclic CMP
CDA	Cholesta-8,24-dien-3-ol-4-carboxylate
cdAMP	3’,5’-Cyclic dAMP
CDOL	4-methylcholesta-8,24-diene-3-ol
CDP	CDP
CDPDG	CDPdiacylglycerol
CELLOBe	Cellobiose (extracellular)
CELLOTe	Cellotriose (extracellular)
CELLUe	Cellulose (extracellular)
CELLWALL	Cellwall (1 g dry cellwall)
CERB1	Cerebrin 1
CERB1A	Cerebrin 1(comp. A)
CERB1B	Cerebrin 1(comp. B)
CERB1C	Cerebrin 1(comp. C)
CERB1D	Cerebrin 1(comp. D)
CERB2	Cerebrin 2
CERB2A	Cerebrin 2(comp. A)
CERB2B	Cerebrin 2(comp. B)
CERB2C	Cerebrin 2(comp. C)
CERB2D	Cerebrin 2(comp. D)
CEREB1	Cerebroside 1
CEREB2	Cerebroside 2
cGMP	3’,5’-Cyclic GMP
CHCOA	6-Carboxyhexanoyl-CoA
CHIT	Chitin
CHITO	Chitosan
CHO	Choline
CHOR	Chorismate
CHOSLF	Choline sulphate
CHOSLFe	Choline sulphate (extracellular)
cIMP	3’,5’-Cyclic IMP
CIT	Citrate
CITe	Citrate (extracellular)
CITm	Citrate (mitochondrial)
CITR	L-Citrulline
CITRe	L-Citrulline (extracellular)
CITRm	L-Citrulline (mitochondrial)
CL	Cardiolipin
CLAGL3P	1-acyl-sn-glycerol-3-phosphate used for cardiolipin
CLCDPDG	Cdp-diacylglycerol used for cardiolipin
CLPA	Phosphatidate used for cardiolipin

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Abbreviation	Full name
CLPIGP	3(3-sn-phosphatidyl)-sn-glycerol 1-phosphate used for cardiolipin biosynthesis
CMP	CMP
CO_2	Carbon dioxide
CO_2e	Carbon dioxide (extracellular)
CO_2m	Carbon dioxide (mitochondrial)
COA	Coenzyme A
COAm	Coenzyme A (mitochondrial)
COUM	Coumarate
COUMe	Coumarate (extracellular)
CPAD5P	1-(2-Carboxyphenylamino)-1-deoxy-D-ribulose 5-phosphate
CTP	CTP
CYS	L-Cysteine
CYSe	L-Cysteine (extracellular)
CYST	Cystine
CYTD	Cytidine
CYTS	Cytosine
D6PDGC	6-phospho-2-dehydro-D-gluconate
D6PGC	6-Phospho-D-gluconate
D6PGL	d-Glucono-1,5-lactone 6-phosphate
DA	Deoxyadenosine
DADP	dADP
DAGLY	Diacylglycerol
DAGLYP	Diacylglycerol-3-Phosphate
DAMP	dAMP
DAONA	7,8-diaminononanoate
DATP	dATP
DC	Deoxycytidine
DCDA	4-methylcholesta-8,24-diene-3-ol-4-carboxylate
DCDOL	4,4-Dimethylcholesta-8,24-diene-3-ol
DCDP	dCDP
DCMP	dCMP
DCTOL	4,4-Dimethylcholesta-8,14,24-triene-3-ol
DCTP	dCTP
DG	Deoxyguanosine
DGDG	Digalactosyl diglyceride
DGDMIPC	Digalactosyl-dimannosyl-inositol-P-ceramide
DGDP	dGDP
DGLC	D-Glucose
DGLCe	D-Glucose (extracellular)
DGMP	dGMP
DGTP	dGTP
DHBA	2,3-dihydroxybenzoate
DHCHDDC	(1R,6S)-dihydroxycyclohexa-2,4-diene-1,4-dicarboxylate
DHF	7,8-Dihydrofolate
DHMVAm	(R)-2,3-dihydroxy-3-methylbutanoate (mitochondrial)

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Abbreviation	Full name
DHP	2-Amino-4-hydroxy-6-(D-erythro-1,2,3-trihydroxypropyl)-7,8-dihydropteridine
DHPLYSm	protein-dihydrolipoyllysine
DHPT	Dihydropteroate
DHSK	3-Dehydroshikimate
DHSKe	3-Dehydroshikimate (extracellular)
DHVALm	(R)-2,3-dihydroxy-3-methylbutanoate (mitochondrial)
DIMGP	D-erythro-1-(Imidazol-4-yl)glycerol 3-phosphate
DIN	Deoxyinosine
DMAND	D-mandelate
DMANDe	D-mandelate (extracellular)
DMIPC	Di-mannosyl-inositol-P-ceramide
DMNAD	Deamido-NAD
DMPP	Dimethylallyl diphosphate
DMT	Dimethylterephthalate
DMTe	Dimethylterephthalate (extracellular)
DNA	Deoxyribonucleic acid
DOROA	(S)-Dihydroorotate
DPCOA	Dephospho-CoA
DPTH	2-[3-Carboxy-3-(methylammonio)propyl]-L-histidine
DQT	3-Dehydroquinate
DR1P	Deoxy-ribose 1-phosphate
DSAM	S-Adenosylmethioninamine
DT	Thymidine
DTB	Dethiobiotin
DTBe	dethiobiotin (extracellular)
DTDP	dTDP
DTMP	dTMP
DTTP	dTTP
DU	Deoxyuridine
DUDP	dUDP
DUMP	dUMP
DUTP	dUTP
E	D-Erythrose
E4P	D-Erythrose 4-phosphate
Ee	D-Erythrose (extracellular)
EOL	Erythritol
EOLe	Erythritol (extracellular)
EPST	Episterol
ERGOD	Ergosta-5,7-dienol
ERGOSE	Ergosterolester
ERGOST	Ergosterol
ERGOT	Ergosta-5,7,22,24-tetraenol
ETH	Ethanol
ETHe	Ethanol (extracellular)
ETHm	Ethanol (mitochondrial)

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Abbreviation	Full name
EU	L-Erythrulose
EU1P	L-Erythrulose 1-phosphate
EUe	L-Erythrulose (extracellular)
F26P	D-Fructose 2,6-bisphosphate
F6P	β-D-Fructose 6-phosphate
FADH2m	FADH2 (mitochondrial)
FADm	FAD (mitochondrial)
FALD	Formaldehyde
FDP	β-D-Fructose 1,6-bisphosphate
FER	Ferulic acid
FERCOA	trans-feruloyl-CoA
FERe	Ferulic acid (extracellular)
FERHCOA	4-hydroxy-3-methoxyphenyl-beta-hydroxypropionyl-CoA
FERIm	Ferricytochrome c (mitochondrial)
FEROm	Ferrocytochrome c (mitochondrial)
FEST	Fecosterol
FGAM	2-(Formamido)-N1-(5'-phosphoribosyl)acetamidine
FGAR	5'-Phosphoribosyl-N-formylglycinamide
FGT	S-Formylglutathione
FKYN	L-Formylkynurenine
FOR	Formate
FORe	Formate (extracellular)
FORm	Formate (mitochondrial)
FPP	trans,trans-Farnesyl diphosphate
FRU	D-Fructose
FRUe	D-Fructose (extracellular)
FTHF	10'-Formyltetrahydrofolate
FTHFm	10-Formyltetrahydrofolate (mitochondrial)
FUACAC	4-Fumarylacetoacetate
FUM	Fumarate
FUMe	Fumarate (extracellular)
FUMm	Fumarate (mitochondrial)
G	D-Glycerate
G1P	α-D-Glucose 1-phosphate
G6P	α-D-Glucose 6-phosphate
GA6P	D-Glucosamine 6-phosphate
GABA	4-Aminobutanoate
GABAe	4-Aminobutanoate (extracellular)
GABAm	4-Aminobutanoate (mitochondrial)
GAG	Galactosaminogalactan
GAL1P	α-D-Galactose 1-phosphate
GALCER	Galactosylceramide
GALCERA	Galactosylceramide(Comp. A)
GALCERB	Galactosylceramide(Comp. B)
GALN14LAC	D-Galactono-1,4-lactone
GALNT	D-Galactonate

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Abbreviation	Full name
GALNTe	D-Galactonate (extracellular)
GALOL	Galactitol
GALOLe	Galactitol (extracellular)
GALUNT	D-Galacturonate
GALUNTe	D-Galacturonate (extracellular)
GALUNTP	1-phospho-alpha-D-glucuronate
GAMYLe	Glucoamylase (secreted to the medium)
GAR	5’-Phosphoribosylglycinamide
GBAD	4-Guanidino-butanamide
GBAT	4-Guanidino-butanoate
GC	gamma-L-Glutamyl-L-cysteine
GDMIPC	Galactosyl-Dimannosyl-inositol-P-ceramide
GDP	GDP
GDPm	GDP (mitochondrial)
GDPMAN	GDPmannose
GEN	Gentisate
GGM	Galactoglucomannan
GL	Glycerol
GL3P	Glycerol 3-phosphate
GLAC	D-Galactose
GLACe	D-Galactose (extracellular)
GLAL	Glycolaldehyde
GLC	α-D-Glucose
GLCe	α-D-Glucose (extracellular)
GLCN	D-Glucosamine
GLCN15LAC	d-Glucono-1,5-lactone
GLCN15LACe	d-Glucono-1,5-lactone (extracellular)
GLCNT	D-Gluconate
GLCNTe	D-Gluconate (extracellular)
GLCUNT	D-Glucuronate
GLCUNTe	D-Glucuronate (extracellular)
GLe	Glycerol (extracellular)
GLN	L-Glutamine
GLNe	L-Glutamine (extracellular)
GLU	L-Glutamate
GLUCER1	Glucocerebroside 1
GLUCER2	Glucocerebroside 2
GLUe	L-Glutamate (extracellular)
GLUGSAL	L-Glutamate 5-semialdehyde
GLUGSALm	L-Glutamate 5-semialdehyde (mitochondrial)
GLUm	L-Glutamate (mitochondrial)
GLUP	α-D-Glutamyl phosphate
GLX	Glyoxylate
GLY	Glycine
GLYA	Glycolate
GLYAL	D-Glyceraldehyde

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Abbreviation	Full name
GLYCOGEN	Glycogen
GLYCOGENe	Glycogen (extracellular)
GLYe	Glycine (extracellular)
GLYm	Glycine (mitochondrial)
GLYN	Glycerone (DHA/dihydroxyacetone)
GLYNe	Glycerone (DHA/dihydroxyacetone) (extracellular)
GMP	GMP
GN	Guanine
GNTAL	Gentisate aldehyde
GPP	Geranyl diphosphate
GSN	Guanosine
GTP	GTP
GTPm	GTP (mitochondrial)
GUA	Guaiacol
H^+	Intracellular protons
H^+_PO	Proton (energy metabolism)
H^+_POm	Proton (mitochondrial) (energy metabolism)
H^+e	Protons (extracellular)
H_2O	Water
H_2O_2	Hydrogen peroxide
H_2O_2e	Hydrogen peroxide (extracellular)
H_2Oe	Water (extracellular)
H_2Om	Water (mitochondria)
H2S	Hydrogen sulfide
H_2SO_3	Sulfite
H_2SO_3e	Sulfite (extracellular)
H3MCOA	(S)-3-Hydroxy-3-methylglutaryl-CoA
HACNm	But-1-ene-1,2,4-tricarboxylate (mitochondrial)
HAN	3-Hydroxyanthranilate
HCITm	2-Hydroxybutane-1,2,4-tricarboxylate (mitochondrial)
HCYS	L-Homocysteine
HICITm	Homoisocitrate (mitochondrial)
HIS	L-Histidine
HISe	L-Histidine (extracellular)
HISN	Histamine
HISOL	L-Histidinol
HISOLP	L-Histidinol phosphate
HIUR	5-hydroxyisourate
HKYN	3-Hydroxykynurenine
HNO_2	Nitrite
HNO_3	Nitrate
HNO_3e	Nitrate (extracellular)
HOMOGEN	Homogentisate
HPLYSm	H-protein-lipoyllysine
HPSAMLYSm	H-protein-S-aminomethyldihydrolipoyllysine
HSER	L-Homoserine

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Abbreviation	Full name
HYXN	Hypoxanthine
HYXNe	Hypoxanthine (extracellular)
ICIT	Isocitrate
ICITe	Isocitrate (extracellular)
ICITm	Isocitrate (mitochondrial)
IDOL	L-Iditol
IDOLe	L-Iditol (extracellular)
IDP	IDP
IDPm	IDP (mitochondrial)
IGP	Indoleglycerol phosphate
ILE	L-Isoleucine
ILEe	L-Isoleucine (extracellular)
ILEm	L-Isoleucine (mitochondrial)
IMACP	3-(Imidazol-4-yl)-2-oxopropyl phosphate
IMASP	Iminoaspartate
IMP	IMP
INAC	Indoleacetate
IND	Indole
INDe	Indole (extracellular)
INS	Inosine
IPC	Inositol phosphorylceramide
IPPMALm	2-Isopropylmalate (mitochondrial)
IPPP	Isopentenyl diphosphate
ITP	ITP
ITPm	ITP (mitochondrial)
KDDGC	2-dehydro-3-deoxy-D-gluconate
KOJA	Kojic acid
KOJAe	Kojic acid (extracellular)
KYN	L-Kynurenine
KYNe	L-Kynurenine (extracellular)
LAC	D-Lactate
LACAL	D-Lactaldehyde
LACe	D-Lactate (extracellular)
LACm	(R)-Lactate (mitochondrial)
LACT	Lactose
LACTe	Lactose (extracellular)
LAOL	L-Arabitol
LAOLe	L-Arabitol (extracellular)
LARAB	L-Arabinose
LARABe	L-Arabinose (extracellular)
LEU	L-Leucine
LEUe	L-Leucine (extracellular)
LEUm	L-Leucine (mitochondrial)
LGT	S-D-Lactoylglutathione
LIPIDS	Artificial metabolite. The metabolites found in the biomass. Measured in grams

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Abbreviation	Full name
LIPOm	Lipoamide (mitochondrial)
LLAC	L-Lactate
LLACe	L-Lactate (extracellular)
LLACm	(S)-Lactate (mitochondrial)
LLCT	L-Cystathionine
LMAND	L-mandelate
LMANDe	L-mandelate (extracellullar)
LNST	Lanosterol
LPC	Lysophosphatidylcholine
LPE	Lysophosphatidylethanolamine
LPSE2m	(LipS2)-dihydrolipoyl transsuccinylase
LXUL	L-Xylulose
LXULe	L-Xylulose (extracellular)
LYS	L-Lysine
LYSe	L-Lysine (extracellular)
LYSm	L-Lysine (mitochondrial)
MACAC	maleylacetoacetate
MAGLY	Monoacylglycerol
MAGLYP	Monoacylglycerol-3-Phosphate
MAL	(S)-Malate
MALACP	Malonyl-[acyl-carrier protein]
MALCOA	Malonyl coenzyme A
MALe	(S)-Malate (extracellular)
MALm	(S)-Malate (mitochondrial)
MAN	D-Mannose
MAN1P	α-D-Mannose 1-phosphate
MAN6P	D-Mannose 6-phosphate
MANe	D-Mannose (extracellular)
MANNANe	Mannan (extracellular)
MELIe	Melibiose (extracellular)
MET	L-Methionine
METe	L-Methionine (extracellular)
METH	Methanethiol
METHF	5,10-Methenyltetrahydrofolate
METHFm	5,10-Methenyltetrahydrofolate (mitochondrial)
METHOL	Methanol
METHOLe	Methanol (extracellular)
METTHF	5,10-Methylenetetrahydrofolate
METTHFm	5,10-Methylenetetrahydrofolate (mitochondrial)
MGC181	Monoglucosyloxyoctadecenoic acid
MGDG	Monogalactosyl diglyceride
MI1P	1L-myo-Inositol 1-phosphate
MIPC	Mannose-inositol-P-ceramide
MLT	Maltose
MLTe	Maltose (extracellular)
MNT	D-Mannitol

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Abbreviation	Full name
MNT1P	D-Mannitol 1-phosphate
MNTe	D-Mannitol (extracellular)
MTHF	5-Methyltetrahydrofolate
MTHFm	5-Methyltetrahydrofolate (mitochondrial)
MTHGXL	Methylglyoxal
MTPHTH	Monomethylterephthalate
MUCL	Muconolactone
MUCO	cis,cis-muconate
MVL	(R)-Mevalonate
MYOI	myo-Inositol
NAD	NAD+
NADH	NADH
NADHm	NADH (mitochondrial)
NADm	NAD+ (mitochondrial)
NADP	$NADP^+$
NADPH	NADPH
NADPHm	NADPH (mitochondrial)
NADPm	$NADP^+$ (mitochondrial)
NAG	N-Acetyl-D-glucosamine
NAGA1P	N-Acetyl-D-glucosamine 1-phosphate
NAGA6P	N-Acetyl-D-glucosamine 6-phosphate
NAGLUm	N-Acetyl-L-glutamate (mitochondrial)
NAGLUPm	N-Acetyl-L-glutamate 5-phosphate (mitochondrial)
NAGLUSm	N-Acetyl-L-glutamate 5-semialdehyde (mitochondrial)
NAHISN	N-acetylhistamine
NAMN	Nicotinate D-ribonucleotide
NAMR	Nicotinamide D-ribonucleoside
NAORNm	N2-Acetyl-L-ornithine (mitochondrial)
NAR	Nicotinate D-ribonucleoside
NFAN	N-formylanthranilate
NH_3	Ammonia
NH_3e	Ammonia (extracellular)
NH_3m	Ammonia (mitochondrial)
NH_4OH	Ammonium hydroxide
NICA	Nicotinate
NICAe	Nicotinate (extracellular)
NICD	Nicotinamide
NICDe	Nicotinamide (extracellular)
NIG	Nigeran (alpha-1,3-Glucose-alpha-1,4-Glucose)
NMN	Nicotinamide D-ribonucleotide
NPRAN	N-(5-Phospho-D-ribosyl)anthranilate
O_2	Oxygen
O_2e	Oxygen (extracellular)
O_2m	Oxygen (mitochondrial)
OA	Oxaloacetate
OAe	Oxaloacetate (extracellular)

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Abbreviation	Full name
OAEL	3-Oxoadipate enol-lactone
OAHSER	O-Acetyl-L-homoserine
OAm	Oxaloacetate (mitochondrial)
OBUT	2-Oxobutanoate
OBUTm	2-Oxobutanoate (mitochondrial)
OGT	Oxidized glutathione
OICAP	3-Carboxy-4-methyl-2-oxopentanoate
OICAPm	3-Carboxy-4-methyl-2-oxopentanoate (mitochondrial)
OIVALm	(R)-2-Oxoisovalerate (mitochondrial)
OMP	Orotidine 5’-phosphate
OMVAL	3-Methyl-2-oxobutanoate
OMVALm	3-Methyl-2-oxobutanoate (mitochondrial)
ORN	L-Ornithine
ORNe	L-Ornithine (extracellular)
ORNm	L-Ornithine (mitochondrial)
OROA	Orotate
OTA	Ochratoxin A
OTAe	Ochratoxin A (extracellular)
OTHIO	Oxidized thioredoxin
OTHIOm	Oxidized thioredoxin (mitochondrial)
OXAL	Oxalate
OXALe	Oxalate (extracellular)
OXAm	Oxaloglutarate (mitochondrial)
OXGLY	Oxaloglycolate
P5C	(S)-1-Pyrroline-5-carboxylate
P5Cm	(S)-1-Pyrroline-5-carboxylate (mitochondrial)
PABA	4-Aminobenzoate
PANT	(R)-Pantoate
PAP	Adenosine 3’,5’-bisphosphate
PAPS	3’-Phosphoadenylylsulfate
PC	Phosphatidylcholine
PCAGL3P	1-acyl-sn-glycerol-3-phosphate used for phosphatidylcholine
PCAT3P2	1-acyl-sn-glycerone phosphate used for phosphatidylcholine
PCC	Protocatechuate
PCCDPDG	Cdp-diacylglycerol used for phosphatidylcholine
PCCe	Protocatechuate (extracellular)
PCPA	Phosphatidate used for phosphatidylcholine
PCPDME	Phosphatidyl-N-dimethylethanolamine
PCPE	Phosphatidylethanolamine used for phosphatidylcholine
PCPMME	Phosphatidyl-N-methylethanolamine
PCPS	Phosphatidylserine used for phosphatidylcholine
PE	Phosphatidylethanolamine
PEAGL3P	1-acyl-sn-glycerol-3-phosphate used for phosphatidylethanolamine
PEAT3P2	1-acyl-sn-glycerone phosphate used for phosphatidylethanolamine
PECDPDG	Cdp-diacylglycerol used for phosphatidylethanolamine
PECTATEe	Pectate (extracellular)

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Abbreviation	Full name
PENAL	Pentanal
PENN	Pentylamine
PENNe	Pentylamine (extracellular)
PEP	Phosphoenolpyruvate
PEPA	Phosphatidate used for phosphatidylethanolamine
PEPS	Phosphatidylserine used for phosphatidylethanolamine
PG	Phosphatidylglycerol
PHAC	Phenylacetate
PHACe	Phenylacetate (extracellular)
PHAL	Phenylacetaldehyde
PHALe	Phenylacetaldehyde (extracellular)
PHE	L-Phenylalanine
PHEe	L-Phenylalanine (extracellular)
PHEN	Prephenate
PHP	3-Phosphonooxypyruvate
PHPYR	Phenylpyruvate
PHPYRe	Phenylpyruvate (extracellular)
PHSER	O-Phospho-L-homoserine
PI	Orthophosphate
PIe	Orthophosphate (extracellular)
PIm	Orthophosphate (mitochondrial)
PINS	1-Phosphatidyl-D-myo-inositol
PINSP	1-Phosphatidyl-1D-myo-inositol 3-phosphate
PMVL	(R)-5-Phosphomevalonate
PNTO	(R)-Pantothenate
POOL	Artificial metabolite. A group of small molecules found in the biomass
PPI	Pyrophosphate
PPIm	Pyrophosphate (mitochondrial)
PPMVL	(R)-5-Diphosphomevalonate
PRAM	5-Phosphoribosylamine
PRBAMP	N1-(5-Phospho-D-ribosyl)-AMP
PRBATP	N1-(5-Phospho-D-ribosyl)-ATP
PRCP	5-Phosphoribosyl monophosphate
PRFICA	1-(5’-Phosphoribosyl)-5-formamido-4-imidazolecarboxamide
PRFP	5-(5-Phospho-D-ribosylaminoformimino)-1-(5-phosphoribosyl)-imidazole-4-carboxamide
PRLP	N-(5’-Phospho-D-1’-ribulosylformimino)-5-amino-1-(5"-phospho-D-ribosyl)-4-imidazolecarboxamide
PRO	L-Proline
PROe	L-Proline (extracellular)
PROm	L-Proline (mitochondrial)
PROP	Propanoate
PROPACP	Propanoyl-[acyl-carrier protein]
PROPAL	Propionaldehyde
PROPALe	Propionaldehyde (extracellular)
PROPCOA	Propanoyl-CoA

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Abbreviation	Full name
PROPCOAm	Propanoyl-CoA (mitochondrial)
PROPe	Propanoate (extracellular)
PROPm	Propanoate (mitochondrial)
Protein	Protein
PRPP	5-Phospho-alpha-D-ribose 1-diphosphate
PS	Phosphatidylserine
PSAGL3P	1-acyl-sn-glycerol-3-phosphate used for phosphatidylserine
PSAT3P2	1-acyl-sn-glycerone phosphate used for phosphatidylserine
PSCDPDG	Cdp-diacylglycerol used for phosphatidylserine
PSNIG	Pseudonigeran (1,3-alpha-glucan)
PSPA	Phosphatidate used for phosphatidylserine
PYR	Pyruvate
PYRe	Pyruvate (extracellular)
PYRm	Pyruvate (mitochondrial)
QH_2m	Ubiquinol (mitochondrial)
Qm	Ubiquinone (mitochondrial)
QT	Quinate
QTe	Quinate (extracellular)
QUIN	Quinolinate
QUINe	Quinolinate (extracellular)
R1P	D-Ribose 1-phosphate
R5P	D-Ribose 5-phosphate
RAFFe	Raffinose (extracellular)
RES	Resocinol
RESe	Resocinol (extracellular)
RGT	Glutathione
RHA	L-Rhamnose
RHAe	Extracellular rhamnose
RHAMN	L-rhamnulose
RHAMNP	L-rhamnulose 1-phosphate
RIB	D-Ribose
RIBe	D-Ribose (extracellular)
RIBOL	Ribitol
RIBOLe	Ribitol (extracellular)
RL	D-Ribulose
RL5P	D-Ribulose 5-phosphate
RLe	D-Ribulose (extracellular)
RNA	Ribonucleic acid
RTHIO	Reduced thioredoxin
RTHIOm	Reduced thioredoxin (mitochondrial)
S	Sulfur
S23E	(S)-2,3-Epoxysqualene
S7P	Sedoheptulose 7-phosphate
SACPm	Saccharopine (mitochondrial)
SAH	S-Adenosyl-L-homocysteine
SAICAR	1-(5’-Phosphoribosyl)-5-amino-4-(N-succinocarboxamide)-imidazole

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Abbreviation	Full name
SALI	Salicylate
SALIe	Salicylate (extracellular)
SAM	S-Adenosyl-L-methionine, S-Adenosyl-L-methionine; Acylcarnitine
SAMOB	S-adenosyl-4-methylthio-2-oxobutanoate
SEDAG	1,2-diacyl-sn-glycerol (for Sterolesters)
SEDAGP	1,2-diacyl-sn-glycerol 3-phosphate (for Sterolesters)
SEMAG	Monoacylglycerol(for Sterolesters)
SEMAGP	Monoacylglycerol-3-phosphate (for Sterolesters)
SER	L-Serine
SERe	L-Serine (extracellular)
SLF	Sulfate
SLFe	Sulphate (extracellular)
SME	Shikimate
SME3P	Shikimate 3-phosphate
SMEe	Shikimate (extracellular)
SOR	L-Sorbose
SORe	L-Sorbose (extracellular)
SOT	D-Sorbitol
SOTe	D-Sorbitol (extracellular)
SQL	Squalene
STACe	Stachyose
STARe	Starch (extracellular)
SUCC	Succinate
SUCCe	Succinate (extracellular)
SUCCm	Succinate (mitochondrial)
SUCCOAm	Succinyl coenzyme A (mitochondrial)
SUCCSALm	Succinate-semialdehyde (mitochondrial)
SUCe	Sucrose (extracellular)
T3P1	D-Glyceraldehyde 3-phosphate
T3P2	Glycerone phosphate (DHAP)
TAGLY	Triacylglycerol
TANAe	Tannic acid (extracellular)
TAR	Tartrate
TARe	Tartrate (extracellular)
TDPE1m	(thiamine diphosphate)-alpha-ketoglutarate dehydrogenase
TGDMIPC	Trigalactosyldimannosylinositol-P-ceramide
THF	Tetrahydrofolate
THFG	Tetrahydrofolyl-[Glu](n)
THFm	Tetrahydrofolate (mitochondrial)
THR	L-Threonine
THRe	L-Threonine (extracellular)
THRm	L-Threonine (mitochondrial)
THY	Thymine
TPHTH	Terephthalate
TPHTHe	Terephthalate (extracellular)
TRE	α,α-Trehalose

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Abbreviation	Full name
TRE6P	α,α-Trehalose 6-phosphate
TREe	α,α-Trehalose (extracellular)
TRP	L-Tryptophan
TRPe	L-Tryptophan (extracellular)
TYR	L-Tyrosine
TYRe	L-Tyrosine (extracellular)
UDP	UDP
UDPG	UDPglucose
UDPGAL	UDPgalactose
UDPGALU	UDP-galacturonate
UDPNAG	UDP-N-acetyl-D-glucosamine
UDPNAGAL	UDP-N-acetyl-D-galactosamine
UGC	(-)-Ureidoglycolate
UMP	UMP
URA	Uracil
URAe	Uracil (extracellular)
UREA	Urea
UREAC	Urea-1-carboxylate
UREAe	Urea (extracellular)
UREAm	Urea (mitochondrial)
URI	Uridine
URIC	Ureate
URIe	Uridine (extracellular)
UTP	UTP
VAL	L-Valine
VALe	L-Valine (extracellular)
VALm	L-Valine (mitochondrial)
VAN	Vanillate
VANe	Vanillate (extracellular)
VANIN	Vanillin
XAN	Xanthine
XANe	Xanthine (extracellular)
XMP	Xanthosine 5’-phosphate
XOL	Xylitol
XOLe	Xylitol (extracellular)
XTSINE	Xanthosine
XUL	D-Xylulose
XUL5P	D-Xylulose 5-phosphate
XULe	D-Xylulose (extracellular)
XYL	D-Xylose
XYLANe	Xylan (extracellular)
XYLe	D-Xylose (extracellular)
ZYMST	Zymosterol

Table A.3: Protein composition of *A. niger*. The measured values are from Christias et al. (1975). It is assumed that the ASP/ASN and GLU/GLN ratios are 3:1 as in Oura (1972). Polymerization cost is calculated from Ingraham et al. (1983). A large proportion of the weight of a glycoprotein can be sugar (Leskovac et al. (2005) reports as much as 10–16 % of the weight of glucose oxidase) but data on an average ratio of sugar/protein is neither available nor easily estimated.

Amino acid	**Amount** [$^{\text{mmole}}/_{\text{g protein}}$]
ALA	1.048
ARG	0.419
ASN	0.213
ASP	0.638
CYS	0.080
GLU	0.913
GLN	0.304
GLY	0.875
HIS	0.208
ILE	0.402
LEU	0.715
LYS	0.660
MET	0.107
PHE	0.317
PRO	0.448
SER	0.638
THR	0.510
TRP	0.128
TYR	0.208
VAL	0.544
Polymerization cost:	
ATP	39.729

Table A.4: RNA composition of *A. niger*. The measured values are from Uryson and Belozerskii (1960). Polymerization cost is calculated from Ingraham et al. (1983).

Ribonucleotide	**Amount** $^{mmole}/_{g\ RNA}$
AMP	0.773
GMP	0.931
CMP	0.773
UMP	0.615
Polymerization cost:	
ATP	7.424

Table A.5: DNA composition of *A. niger*. The measured values are from Uryson and Belozerskii (1960) and in accordance with the ratio of the genome sequence of CBS 513.88 (Pel et al., 2007). Polymerization cost is calculated from Ingraham et al. (1983).

Deoxyribonucleotides	**Amount** $^{mmol}/_{g\ DNA}$
dAMP	0.782
dCMP	0.814
dTMP	0.782
dGMP	0.814
Polymerization cost:	
ATP	10.849

Table A.6: Small molecules in the biomass of *A. niger*. The references from which the values are calculated, are found next to each component.

Component	**Reference**	**Amount** $^{mmol}/_{g\ DW}$
Isocitrate	Promper et al. (1993)	0.075
Citrate	Promper et al. (1993)	2.498
Succinate	Promper et al. (1993)	0.107
Fumarate	Promper et al. (1993)	0.008
Malate	Promper et al. (1993)	0.087
NAD	Fuhrer et al. (1980)	1.128
NADH	Fuhrer et al. (1980)	0.120
NADP	Fuhrer et al. (1980)	0.104
NADPH	Fuhrer et al. (1980)	0.060
Trehalose	Witteveen and Visser (1995)	13.692
Mannitol	Witteveen and Visser (1995)	32.791
Glycerol	Witteveen and Visser (1995)	42.363
Erythritol	Witteveen and Visser (1995)	36.636
Arabitol	Witteveen and Visser (1995)	1.521

Table A.7: Cell wall composition of *A. niger*. The references from which the values are calculated, are found next to each component.

Cell wall component	**Reference**	**Amount** $^{\text{mmol}}/_{\text{g cell wall}}$
Galactosaminogalactan	Bardalaye and Nordin (1976)	0.04
Nigeran	Johnston (1965), Damveld et al. (2005)	0.25
Pseudonigeran (α-1,3-glucan)	Horisberger et al. (1972)	0.33
Galactoglucomannan	Bardalaye and Nordin (1977), Horisberger et al. (1972)	0.37
1,4-α-glucan	Stagg and Feather (1973)	0.38
Chitin	Ram et al. (2004), Stagg and Feather (1973), Blumenthal and Roseman (1957)	1.57
1,3-β-glucan	Stagg and Feather (1973), Ram et al. (2004)	2.64

Table A.8: Lipid composition of *A. niger*. The amounts are sorted into categories of neutral lipids, sphingolipids and phospholipids. The references from which the values are calculated, are found next to each component.

Lipids	**Reference**	**Amount** mmol/g DW
Neutral lipids		
Triacylglycerols	Morozova et al. (2002)	0.010083
Diacylglycerols	Morozova et al. (2002)	0.001009
Monoacylglycerols	Morozova et al. (2002)	0.008912
C14:0 acyl	Morozova et al. (2002)	0.000223
C16:0 acyl	Morozova et al. (2002)	0.001480
C18:0 acyl	Morozova et al. (2002)	0.000245
C18:1 acyl	Morozova et al. (2002)	0.001678
C18:2 acyl	Morozova et al. (2002)	0.001664
C18:3 acyl	Morozova et al. (2002)	0.000047
Ergosterol	Nemec and Jernejc (2002)	0.034062
Ergosterol esters	Nemec and Jernejc (2002)	0.010038
Glucolipids		
Monogalactosyldiglyceride	Chattopadhyay et al. (1985a)	0.030053
Monoglucosyloxyoctadecenoic acid	Brennan et al. (1974)	0.012374
Digalactosyldiglyceride	Chattopadhyay et al. (1985a)	0.007859
Sphingolipids		
Trigalactosyldimannosylinositol-phosphorylceramide (GPSL G)	Byrne and Brennan (1976)	0.000005
Cerebrin 1 (with C18 or C20 Phytosphingosin)	Byrne and Brennan (1976)	0.000030
Cerebrin 2 (with C18 or C20 sphingosin)	Byrne and Brennan (1976)	0.000031
Cerebroside (Galactosylceramide)	Byrne and Brennan (1976)	0.000025
Glucocerebroside 1	Byrne and Brennan (1976)	0.000024
Glucocerebroside 2	Byrne and Brennan (1976)	0.000024
Phospholipids		
Cardiolipin	Chattopadhyay et al. (1985a)	0.001746
Phosphatidylcholine	Chattopadhyay et al. (1985a)	0.015312
Phosphatidylserine	Chattopadhyay et al. (1985a)	0.000359
Phosphatidylethanolamine	Chattopadhyay et al. (1985a)	0.034807

Table A.9: Carbon sources found in literature available to the model. Substrates that are only found as carbon sources together with glucose are indicated by ∗.

C-source		Reference
Acetate		Ruijter et al. (1999)
Alanine	∗	Nomachi and Komano (1980)
Anthranilic acid	∗	Reddy and Vaidyanathan (1975)
Arabinose		vanKuyk et al. (2001), de Groot et al. (2003), de Vries et al. (2002b), Witteveen et al. (1994)
Arabitol		vd Veen et al. (1993)
Aspartic acid	∗	Nomachi and Komano (1980)
Benzoate	∗	Reddy and Vaidyanathan (1975)
Benzyl-vanillic acid	∗	Milstein et al. (1988)
Citrate		Muller (1975a)
Coumaric acid	∗	Milstein et al. (1988)
Dethiobiotin	∗	Tepper et al. (1966), Li et al. (1968)
D-galacturonic acid		de Vries et al. (2002b), de Vries et al. (2002)
D-glucuronic acid		de Vries et al. (2002b), de Vries et al. (2002)
Dihydroxyacetone		Witteveen et al. (1990a)
Dimethylterephthalate		Ganji et al. (1995)
DL-mandelic acid	∗	Jamaluddin et al. (1970)
D-xylose		Ngiam et al. (2000)
Ferulic acid		Milstein et al. (1988)
Fructose		Ruijter et al. (1999), de Vries et al. (2002b)
Fumarate		Muller (1975a)
Galactose		Ademark et al. (2001a), Basten et al. (2005), de Vries et al. (2002b)
Gluconate		Elzainy et al. (1973), Ruijter et al. (1999)
Gluconic acid lactone		Lakshminarayana et al. (1969a)
Glucose		Numerous
Glutamate	∗	Nomachi and Komano (1980)
Glycerol		Tereshina et al. (2004)
Indole	∗	Kamath and Vaidyanathan (1990)
Lactose		Arisan-Atac et al. (1996)
L-rhamnose		Fries and Kallstromer (1965)
Maltose		Pedersen et al. (2000c)
Mannitol		Tereshina et al. (2004)
Mannose		Adya and Elbein (1977), de Vries et al. (2002b)
Methanol		Kirimura et al. (1999)
m-hydroxybenzoic acid	∗	Premkumar et al. (1969), Kumar et al. (1973)
Phenylacetic acid	∗	Sugumaran et al. (1973)
Phenylalanine	∗	Kishore et al. (1974, 1976)
Resorcinol		Shailubhai et al. (1983)
Rhamnose		de Vries et al. (2002b)
Salicylate		Shailubhai et al. (1983)
Sorbitol		Desai et al. (1967, 1969a), vd Veen et al. (1991)
Succinate		Muller (1975a)
Sucrose		Arisan-Atac et al. (1996), de Graaff et al. (1992)

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C-source		Reference
Tannic acid		Bhardwaj et al. (2003)
Tartrate		Patil and Ramakrishnan (1966)
Trehalose		Tereshina et al. (2004)
Tryptophan	∗	Sreeleela et al. (1969), Subramanian and Vaidyanathan (1984)
Vanillic acid	∗	Milstein et al. (1988)
Xylitol		vd Veen et al. (1993)
Xylose		Ngiam et al. (2000)

Table A.10: Sole carbon sources that are utilizable by *A. niger iMA871, but with no available reference.*

Carbon source
3-hydroxybenzoate
Arginine
Asparagine
Benzonitrile
Benzoylamine
Butanoate
Citrulline
Decanoate
D-Erythrose
D-Lactate
D-mandelate
D-Ribose
D-Ribulose
D-Xylulose
Dodecanoate
Eicosanoate
Ethanol
GABA
Galactitol
Galactonate
Galacturonate
Glutamine
Glycine
Heptadecanoate
Heptadecenoate
Hexadecadienoate
Hexadecanoate
Hexadecenoate
Hexanoate
Isocitrate
L-Arabinose
L-Arabitol
L-Erythrulose
L-Iditol
L-Lactate
L-mandelate
L-Sorbose
L-Xylulose
Malate
Melibiose
Nonadecadienoate
Nonadecanoate
Nonadecenoate
Octadecadienoate
Octadecanoate

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Carbon source
Octadecatrienoate
Octadecenoate
Octanoate
Ornithine
Oxalate
Oxaloacetate
Pentadecanoate
Phenylpyruvate
Proline
Propanoate
Protocatechuate
Pyruvate
Raffinose
Ribitol
Serine
Stachyose
Terephthalate
Tetradecanoate
Tetradecenoate
Threonine
Tyrosine

Table A.11: Compounds utilizable by *A. niger iMA871 as sole nitrogen source. Compounds, where the use as sole nitrogen source has found described in literature, are followed by one or more references.*

Nitrogen source	Reference
Alanine	Lenouvel et al. (2001)
Ammonia	Basten et al. (2001)
Anthranilate	Kamath et al. (1987)
Arginine	Lenouvel et al. (2001)
Asparagine	Lenouvel et al. (2001), Laine et al. (1972)
Aspartate	
Butylamine	Schilling and Lerch (1995a)
Citrulline	Lenouvel et al. (2002)
GABA	Kumar and Punekar (1998)
Glutamate	Lenouvel et al. (2001)
Glutamine	
Glycine	Morton and Broadbent (1955)
Nitrate	Pedersen and Nielsen (2000)
Ornithine	Lenouvel et al. (2002)
Pentylamine	Schilling and Lerch (1995a)
Phenylalanine	
Proline	Lenouvel et al. (2001)
Serine	
Threonine	
Tryptophan	
Tyrosine	
Urea	Smith et al. (1993)
Xanthin	Taha and Sharabash (1956)

Table A.12: Enzymatic activities that were found in the literature, but not added to the reaction list of *A. niger iMA871*. *References, EC-number and enzyme name is added to the reactions where possible.*

Reaction	EC-no	Enzyme	Source
Degradation of biopolymers			
RNA + H_2O ⇆ 3’-phosphomononucleotides	3.1.27.1	RNase I	Nomachi and Komano (1980)
RNA-bound phospho-guanine + H_2O ⇆ RNA + 3’-phospho-guanine	3.1.27.3	RNase II	Nomachi and Komano (1980)
Extracellular RNA + H_2O ⇆ ribonucleotides	3.1.27.1	ribonuclease	Xiong et al. (2005)
Dinucleoside monophosphates + H_2O ⇆ Nucleotide 5’-phosphate + Nucleoside	3.1.4.1	Cyclic-ribonucleotide phosphomutase-5’-phosphodiesterase (phosphodiesterase I/5’-exonuclease activity)	Chohnan et al. (1994)
DNA + H_2O ⇆ Nucleotide monophosphates	3.1.4.1	Phosphodiesterase I (5’-exonuclease)	Chohnan et al. (1994)
Extracellular proteins + H_2O ⇆ Amino acid components	3.4.11.5	prolyl aminopeptidase (papA)	Basten et al. (2005)
Extracellular proteins + H_2O ⇆ Amino acid components	3.4.14.5	dipeptidyl-peptidase IV (dapB)	Javing et al. (2005)
Extracellular proteins + H_2O ⇆ Amino acid components	3.4.16.5	Carboxypeptidase I	dal Degan et al. (1992)
Extracellular proteins + H_2O ⇆ Amino acid components	3.4.16.5	Carboxypeptidase II	dal Degan et al. (1992)
Extracellular proteins + H_2O ⇆ Amino acid components	3.4.16.5	Serine-type carboxypeptidase F (pepF)	Krishnan and Vijayalakshmi (1985), van den Hombergh et al. (1994)
Extracellular proteins + H_2O ⇆ Amino acid components	PEPC	carboxypeptidase C (pepC)	Frederick et al. (1993)
Extracellular proteins + H_2O ⇆ Amino acid components	3.4.21.61	Kexin	Jalving et al. (2000)
Extracellular proteins + H_2O ⇆ Amino acid components	3.4.23.18	Aspergillopepsin A (I) (pepA)	Mattern et al. (1992)
Extracellular proteins + H_2O ⇆ Amino acid components	3.4.23.19	Aspergillopepsin B (II) (pepB)	Mattern et al. (1992), Huang et al. (2000)
removes AAs from peptide end	3.4.11.2	lysine aminopeptidase	Basten et al. (2001)

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Reaction	EC-no	Enzyme	Source
Peptide with N-terminal aromatic amino acid + $H_2O \Rightarrow$ Peptide + aromatic AA	No EC	phenylalanine peptidase	Basten et al. (2003)
Extracellular tri-acyl glycerol + $H_2O \leftrightarrows$ Di-acyl glycerol + Fatty acid	3.1.1.3	Lipase (extracellular)	Namboodiri and Chattopadhyaya (2000)
Extracellular diacyl glycerol + $H_2O \leftrightarrows$ Mono-acyl glycerol + Fatty acid	3.1.1.3	Lipase (extracellular)	Namboodiri and Chattopadhyaya (2000)
Degradation of complex carbon sources			
Glycyrrhizinate + $H_2O \leftrightarrows$ 1,2-β-D-glucuronosyl-D-glucuronate + Glycyrrhetinate	3.2.1.128	glycyrrhizinate β-glucuronidase	Sasaki et al. (1988)
1,2-β-D-glucuronosyl-D-glucuronate + $H_2O \leftrightarrows$ 2 D-Glucuronate	3.2.1.15	Polygalacturonase	Behere et al. (1993), Acuña-Argüelles et al. (1995), de Vries and Visser (2001), de Vries et al. (2002a)
Extracellular phytate + 4 $H_2O \leftrightarrows$ myo-inositol-di-phosphate + 4 Phosphate	3.1.3.8	3-phytase	Skowronski (1978), van Hartingsveldt et al. (1993), Martinelli and Kinghorn (1994), Wyss et al. (1998, 1999), Nagashima et al. (1999), Dvorakova et al. (2000), Vohra and Satyanarayana (2003), Vats and Banerjee (2005)
Extracellular phytate + 5 $H_2O \leftrightarrows$ Inositol-monophosphate + 5 Phosphate	3.1.3.26	6-phytase	Wyss et al. (1999), Vohra and Satyanarayana (2003), Casey and Walsh (2003)
Aromatic degradations			
2-chlorobenzoate + NADPH + $O_2 \leftrightarrows$ 2-chloro-4-hydroxybenzoate + NADP + H_2O	1.14.13.1	benzoate 4-monooxygenase (benzoate-para-hydroxylase A, bphA)	Sahasrabudhe and Modi (1985)
3-chlorobenzoate + NADPH + $O_2 \leftrightarrows$ 3-chloro-4-hydroxybenzoate + NADP + H_2O	1.14.13.1	benzoate 4-monooxygenase (benzoate-para-hydroxylase A, bphA)	Sahasrabudhe and Modi (1985)
2-hydroxybenzoate + NADPH + $O_2 \leftrightarrows$ 2,4-dihydroxybenzoate + NADP + H_2O	1.14.13.1	benzoate 4-monooxygenase	Faber et al. (2001), Malonek et al. (2004)

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Reaction	EC-no	Enzyme	Source
3-Hydroxyanthranilate + Dihydrobiopterin + H_2O ⇆ Anthranilate + Tetrahydrobiopterin + O_2	1.14.16.3	anthranilate 3-monooxygenase	Subba Rao et al. (1971)
Phenylacetate + O_2 + NADPH ⇆ 3-hydroxy-phenylacetate + H_2O + NADP	No EC	Phenylacetate hydroxylase	Sugumaran and Vaidyanathan (1978)
3-hydroxybenzylalcohol + NADP ⇆ 3-hydroxybenzaldehyde + NADPH	No EC	3-hydroxy benzylalcohol dehydrogenase	Sugumaran et al. (1973)
3-hydroxybenzaldehyde + NAD ⇆ 3HBA + NADH	No EC	3-hydroxy benzylaldehyde dehydrogenase	Sugumaran et al. (1973)
Orcinol + NADH + O_2 ⇆ 2,3,5-trihydroxytoluene + NAD + H_2O	1.14.13.6	orcinol 2-monooxygenase	Sahasrabudhe et al. (1986)
4-nitrophenyl phosphate + H_2O ⇆ 4-nitrophenol + Phosphate	3.1.3.41	4-nitrophenylphosphatase	Versaw et al. (1991)
2-hydroxymuconate semialdehyde ⇆ Catechol + O_2	1.13.11.2	catechol 2,3-dioxygenase	Sahasrabudhe et al. (1986)
Miscellaneous			
Sulcaton + NADH ⇆ sulcatol + NAD	1.1.1.260	sulcatone reductase	Belan et al. (1987)
Propanal + NADPH ⇆ Propanol + NADP	1.1.1.78	Methylglyoxal reductase II	Inoue et al. (1988)
Butanal + NAD + H_2O ⇆ Butanate + NADH	1.2.1.3	Aldehyde dehydrogenase (NAD+)	Kazimirova and Novotelnov (1956)
Heptanal + NAD + H_2O ⇆ Heptanate + NADH	1.2.1.3	Aldehyde dehydrogenase (NAD+)	Kazimirova and Novotelnov (1956)
Quercitin + O_2 ⇒ 2-protocatechuoylphloroglucinol carboxylic acid + CO	1.13.11.2‘	Flavonol 2,4 dioxygenase	Hund et al. (1999)
Phloretin + H_2O ⇆ Phloretate + 1,3,5-Trihydroxybenzene	3.7.1.4	phloretin hydrolase	Minamikawa et al. (1970)
2’,3’-Cyclic AMP ⇆ cyclic AMP	3.1.4.16	Cyclic-ribonucleotide phosphomutase-5’-phosphodiesterase	Chohnan et al. (1994)
2’,3’-Cyclic CMP ⇆ cyclic CMP	3.1.4.16	Cyclic-ribonucleotide phosphomutase-5’-phosphodiesterase	Chohnan et al. (1994)
2’,3’-Cyclic GMP ⇆ cyclic GMP	3.1.4.16	Cyclic-ribonucleotide phosphomutase-5’-phosphodiesterase	Chohnan et al. (1994)

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Reaction	EC-no	Enzyme	Source
2',3'-Cyclic IMP ⇆ cyclic IMP	3.1.4.16	Cyclic-ribonucleotide phosphomutase-5'-phosphodiesterase	Chohnan et al. (1994)
Carbaryl ⇆ 1-hydroxynaphthalene + N-methylcarbamate	No EC	Carbaryl hydrolase	Qing et al. (2003)
Methionine + Glyoxalate ⇆ 4-methylthio-2-oxobutanoate + Glycine	2.6.1.73	L-methionine-glyoxylate transaminase	Oganesyan et al. (2004)
Diacetyl + NADPH ⇆ Acetoin + NADP	1.1.1.72	Glycerol dehydrogenase ($NADP^+$)	Schuurink et al. (1990)
Methylglyoxal + NADPH ⇆ 1-Hydroxy-2-propanone + NADP	1.1.1.72	Glycerol dehydrogenase ($NADP^+$)	Schuurink et al. (1990)
4-hydroxyphenylacetaldehyde oxime + NADPH + O_2 ⇆ 4-hydroxymandelonitrile + NADP + 2 H_2	1.13.14.6	NADPH-cytochrome P450 reductase (cprA)	van den Brink et al. (1996), Malonek et al. (2004)
2 Superoxide + 2 H^+ ⇒ O_2 + H_2O_2	1.15.1.1	Cu,Zn superoxide dismutase	Sugumaran and Vaidyanathan (1978), Holdom et al. (1996)
R-CH_2-NH_2 + H_2O + O_2 ⇆ R-CHO + H_2O_2 + NH_3	1.4.3.4	amine oxidase (flavin-containing)	Schilling and Lerch (1995a)
R-CH_2-NH_2 + H_2O + O_2 ⇆ R-CHO + H_2O_2 + NH_3	1.4.3.6	amine oxidase (copper-containing)	Schilling and Lerch (1995a)
Glycerol triacetate + H_2O ⇆ Glycerol + 3 Acetate	3.1.1.3	triacylglycerol lipase	Hannan (1959)
Chlorogenate + H_2O ⇒ Caffeate + Quinate	3.1.1.42	chlorogenic acid hydrolase	Schobel and Pollmann (1980), Asther et al. (2005)
Several epoxides to their di-ols	3.3.2.3	epoxide hydrolase	Morisseau et al. (1999), Arand et al. (1999)
Serine + Glyoxylate ⇆ 3-hydroxypyruvate + Glycine	2.6.1.45	L-serine-glyoxylate transaminase	Oganesyan et al. (2004)
Serine + Pyruvate ⇆ 3-Hydroxypyruvate + Alanine	2.6.1.51	L-serine-pyruvate transaminase	Oganesyan et al. (2004)
Methionine + Pyruvate ⇆ 4-methylthio-2-oxobutanoate + Alanine	2.6.1.41	L-methionine-pyruvate transaminase	Oganesyan et al. (2004)
Valine + Glyoxylate ⇆ (R)-2-Oxoisovalerate + Glycine	No EC	L-valine-glyoxylate transaminase	Oganesyan et al. (2004)

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Reaction	EC-no	Enzyme	Source
Leucine + Glyoxylate ⇆ 4-Methyl-2-oxopentanoate + Glycine	No EC	L-leucine-glyoxylate transaminase	Oganesyan et al. (2004)
Methylamine + H_2O + O_2 ⇒ NH_3 + Methanal + H_2O_2	1.4.3.4	amine oxidase (flavin-containing)	Schilling and Lerch (1995b)
2-Phenylethylamine + H_2O + O_2 ⇒ 2-phenylethanal + NH_3 + H_2O_2	1.4.3.4	amine oxidase (flavin-containing)	Schilling and Lerch (1995a)
Dopamine + H_2O + O_2 ⇒ (3,4-dihydroxyphenyl)acetaldehyde + NH_3 + H_2O_2	1.4.3.4	amine oxidase (flavin-containing)	Schilling and Lerch (1995a)
Ethylamine + H_2O + O_2 ⇒ Acetaldehyde + NH_3 + H_2O_2	1.4.3.4	amine oxidase (flavin-containing)	Schilling and Lerch (1995a)
Sinigrin + H_2O ⇒ D-Glucose + isothiocyanate	3.2.1.147	Myrosinase	Ohtsuru et al. (1973)
UDP-N-acetyl-D-glucosamine + Dolichyl phosphate ⇆ UMP + N-acetyl-D-glucosaminyl-diphosphodolichol	2.7.8.15	UDP-N-acetylglucosamine: dolichyl-phosphate N-acetylglucosaminephosphotra	Sorensen et al. (2003)
Nitrophenylsulphate + H_2O ⇆ Nitrophenol + Sulphate	3.1.6.1	arylsulfatase	Sakurai et al. (1980)

Table A.13: Pathways that were reported in literature to be present, but not included in the reaction list of *A. niger iMA871.*

Compound	Source
Degradation	
2-heptanone	(Baltazar et al., 1999)
2-nonanone	(Baltazar et al., 1999)
Anthracene	Yogambal and Karegoudar (1997)
Caproic acid	Lewis (1970)
Carbaryl	Qing et al. (2003)
Ceramide-phosphoinositol	Hackett and Brennan (1977)
Cerebrosine	Wagner and Fiegert (1969)
Dolichol	Sorensen et al. (2003)
Naphthalene	Yogambal and Karegoudar (1997)
Orcinol	Sahasrabudhe et al. (1986)
PAH	Sack et al. (1997)
Phenenthrene	Yogambal and Karegoudar (1997), Sack et al. (1997)
Pyrene	Wunder et al. (1994)
Secondary metabolites	
1,1-heptanediol diacetate	Abo-Dahab (2002)
1,4-diaza-2,5-dioxo-3-isobutylbicyclo (4.3.0) nonane	Abo-Dahab (2002)
4,9-dimethyl-furano(2,3h) coumarin	Abo-Dahab (2002)
Amphetamine	Abo-Dahab (2002)
Asperazine	Varoglu et al. (1997), Varoglu and Crews (2000)
Aspergillin	Rawat (1968), Ray and Eakin (1975)
Asperic acid	Varoglu and Crews (2000)
Aspernigrin A	Hiort et al. (2004)
Aspernigrin B	Hiort et al. (2004)
Aurasperone B	Bouras et al. (2005)
Aurasperone C	Bouras et al. (2005)
Aurasperone D	Blumenthal (2004), Samson et al. (2004)
Aurasperone E	Bouras et al. (2005)
Aurasperone F	Bouras et al. (2005)
Bicoumanigrin	Hiort et al. (2004)
Butanoic acid 2-[(difluoroacetyl)amino]-butyl ester	Abo-Dahab (2002)
Cycloleucomelone	Hiort et al. (2004)
Dihydroergotamine	Abo-Dahab (2002)
Flavasperone (Asperxanthone)	Bycroft et al. (1962)
Fonsecin	Bouras et al. (2005)
Fumonisin B_2	Frisvad et al. (2007)
Funalenone	Inokoshi et al. (1999)
hexylitaconic acid	Varoglu and Crews (2000)
Kotanin	Büchi et al. (1971), Samson et al. (2004)
Malformin A_1 (Formerly known as A)	Yukioka and Winnick (1966), Schuster et al. (2002), Blumenthal (2004), Kobbe et al. (1977), Yukioka and Winnick (1966)
Malformin A_2	Schuster et al. (2002), Blumenthal (2004), Kobbe et al. (1977), Yukioka and Winnick (1966)
Malformin B	Schuster et al. (2002), Blumenthal (2004), Kobbe et al. (1977), Yukioka and Winnick (1966)
Malformin C	Kobbe et al. (1977), Varoglu and Crews (2000)
Melanin	McGovern and Bentley (1975)
Mlaviolin	McGovern and Bentley (1975)

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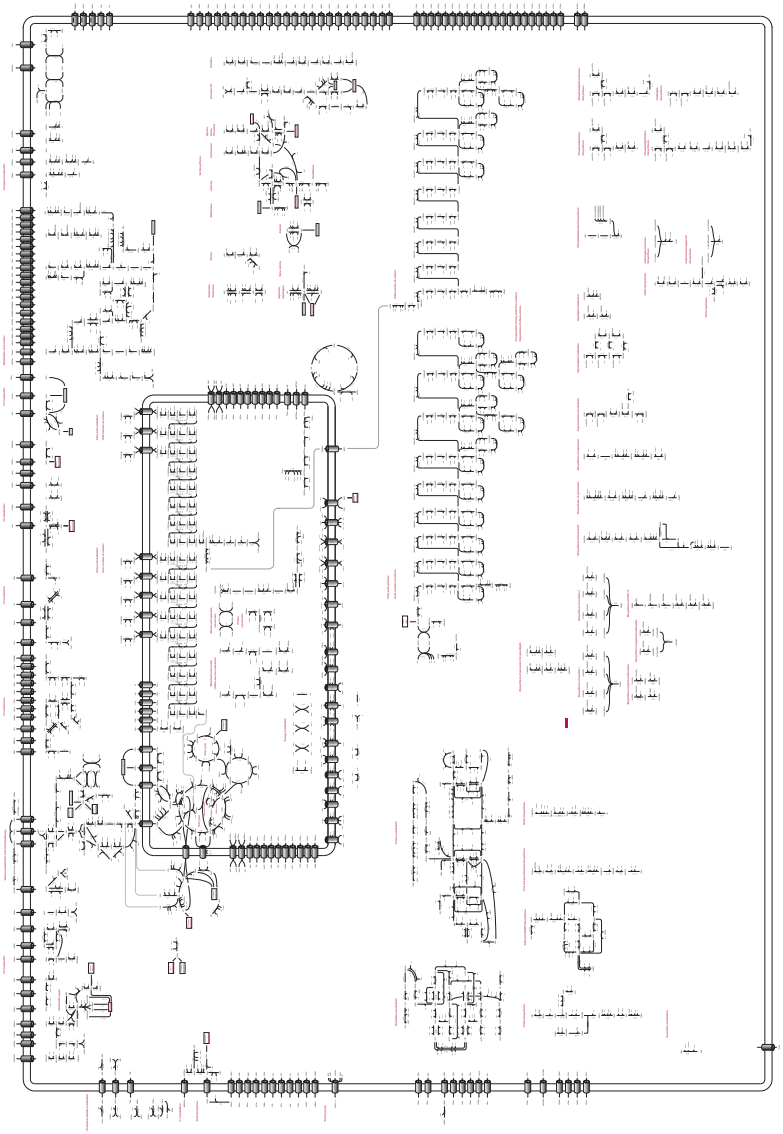
Compound	Source
Nerolidol-epoxyacetate	Abo-Dahab (2002)
n-heptanal	Abo-Dahab (2002)
Nigerazine B	Blumenthal (2004)
Nigragillin	Blumenthal (2004)
N-methylmorpholine	Abo-Dahab (2002)
Ochratoxin A	Abarca et al. (1994), Varga et al. (2003), O'Callaghan et al. (2003), Samson et al. (2004), Blumenthal (2004)
Orlandin	Cutler et al. (1979)
Orobol	Nishioka et al. (1989)
Phatalimide	Abo-Dahab (2002)
Phenol-3,5-dimethoxyphenyl acetate	Abo-Dahab (2002)
Pyranonigrin A	Samson et al. (2004), Hiort et al. (2004)
Pyranonigrin B	Samson et al. (2004), Hiort et al. (2004)
Pyranonigrin C	Samson et al. (2004), Hiort et al. (2004)
Pyranonigrin D	Samson et al. (2004), Hiort et al. (2004)
Pyrophen	Varoglu and Crews (2000)
Roridine E	Abo-Dahab (2002)
Tensidol B	Fukuda et al. (2006)

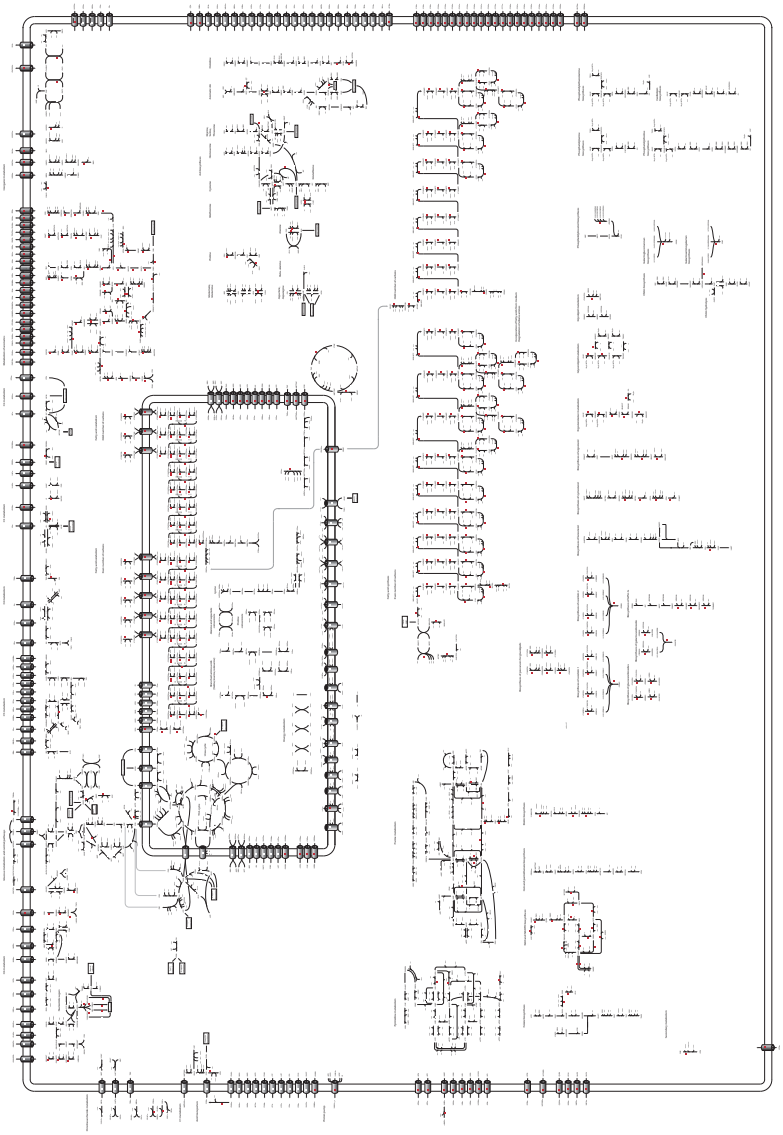
A.1 Metabolic map

Map of all metabolic pathways of the reconstructed metabolic network of chapter 3. Where an EC number for the enzymatic reaction is known, this is noted by the reaction arrow.



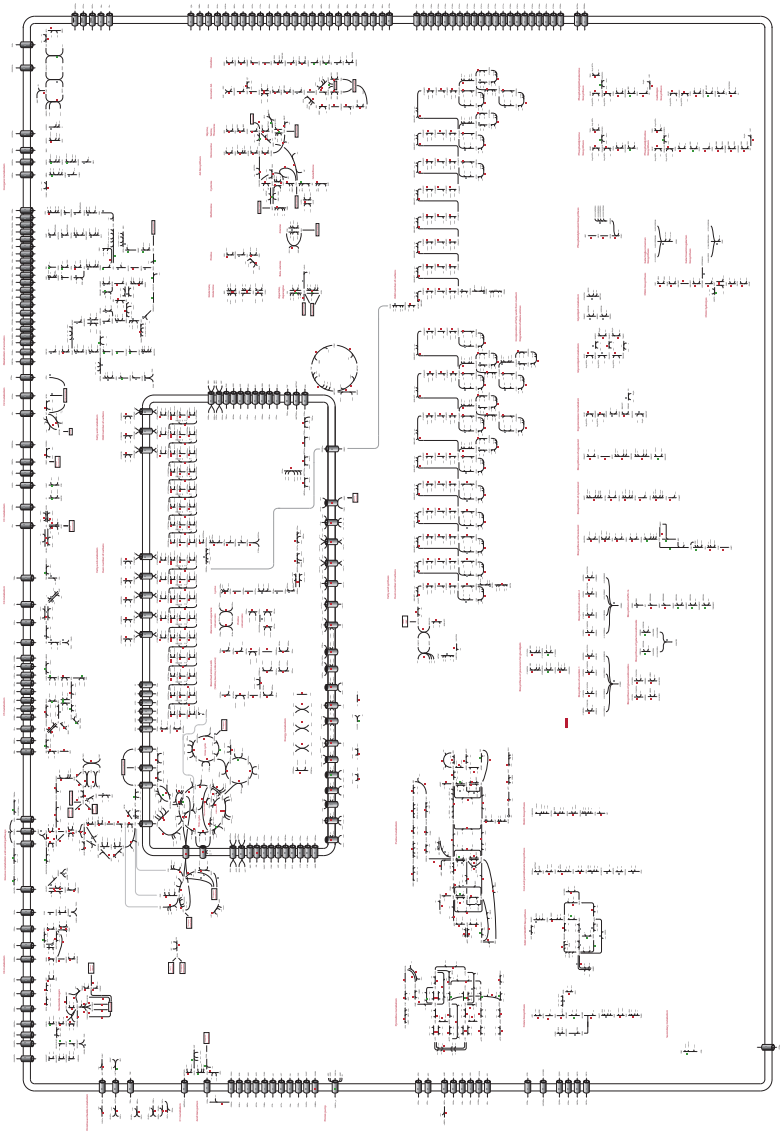
A.2 Map of new reactions

Adaptation of the map of Appendix A.1. Red boxes denote reactions not present in the metabolic models *A. nidulans* *i*HD666 and *A. niger* *i*HD20.



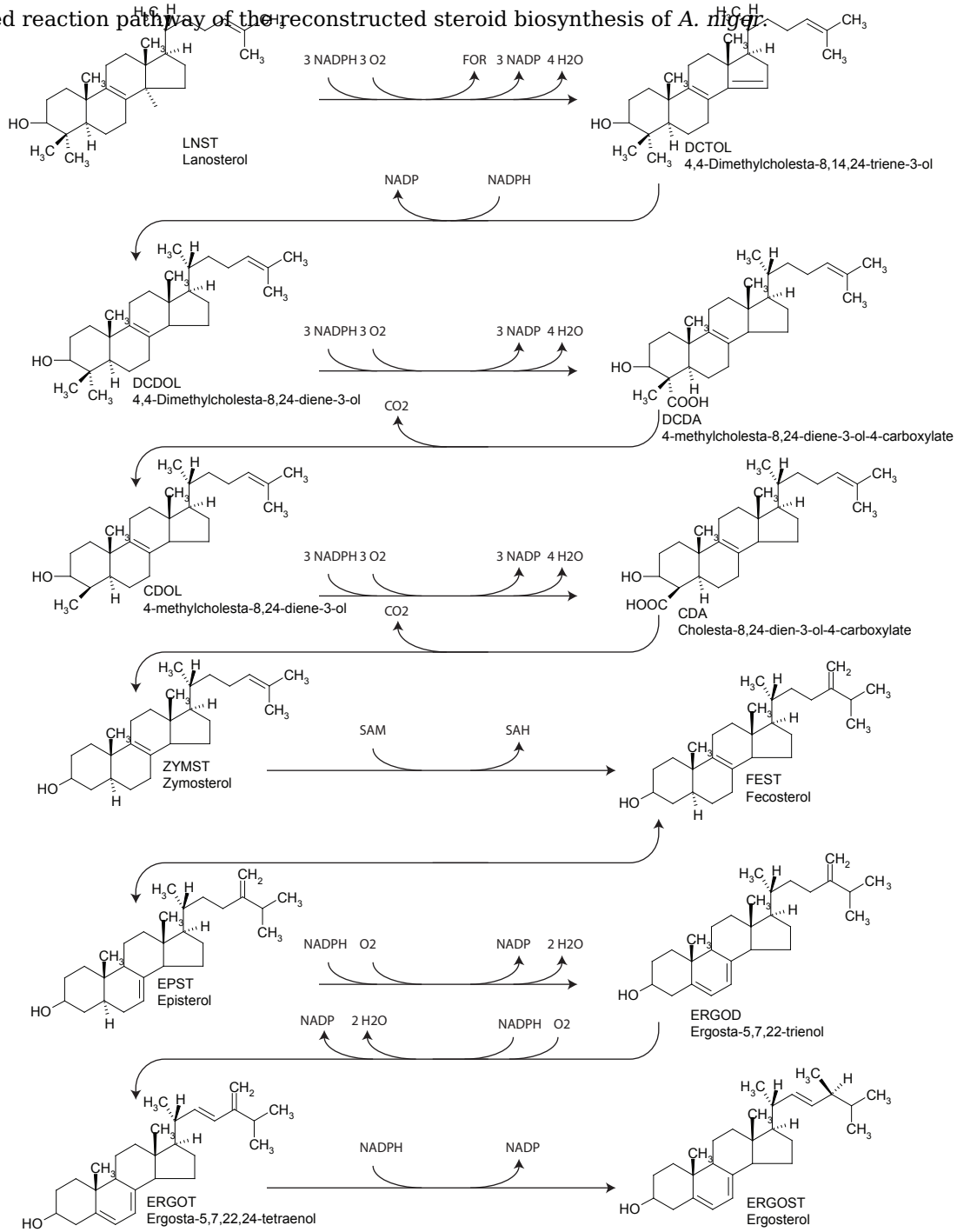
A.3 Transcription response of *A. niger* on glucose and NH_3

Red boxes denote genes that are active in batch cultivations of *A. niger* CBS 513.88 on glucose and NH_3. Gray boxes indicate that no gene for the reaction could be found. White boxes/No box indicate no difference between the strains. Data from Pel et al. (2007).



A.4 Steroid biosynthesis

Detailed reaction pathway of the reconstructed steroid biosynthesis of *A. niger*.



Appendix B

Supplementaries for chapter 4

Table B.1: Assignment of values to unique identifiers in ReMapper maps. This table shows the decisions made by the mapping algorithm when choosing one value for a specific reaction. Result is the result of the previous decisions for that reaction, and Hit is the value of the current gene.

		Result					
		No previous hit	**Up**	**Down**	**NoCh**	**NoORF**	**Mix**
Hit	**Up**	Up	Up	Mix	Up	Up	Mix
	Down	Down	Mix	Down	Down	Down	Mix
	NoCh	NoCh	Up	Down	NoCh	NoCh	Mix
	NoORF	NoORF	Up	Down	NoCh	NoORF	Mix

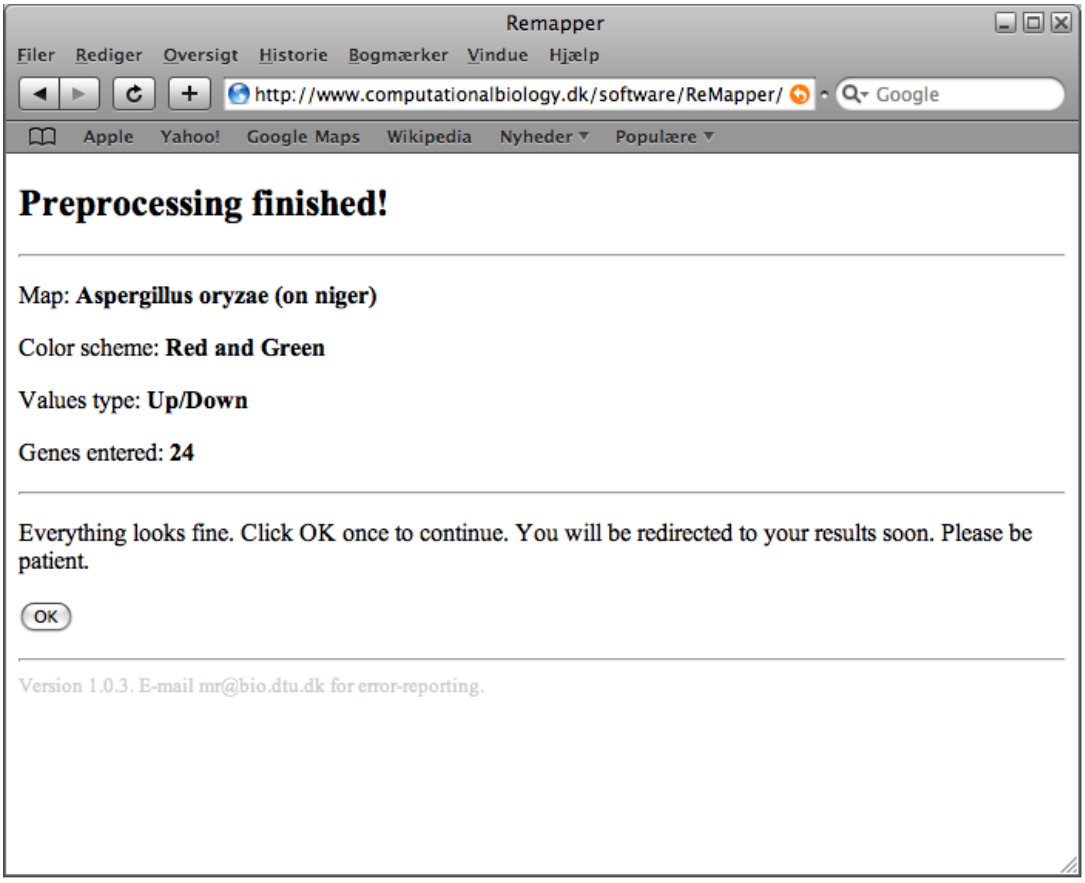


Figure B.1: ReMapper preprocessing results.

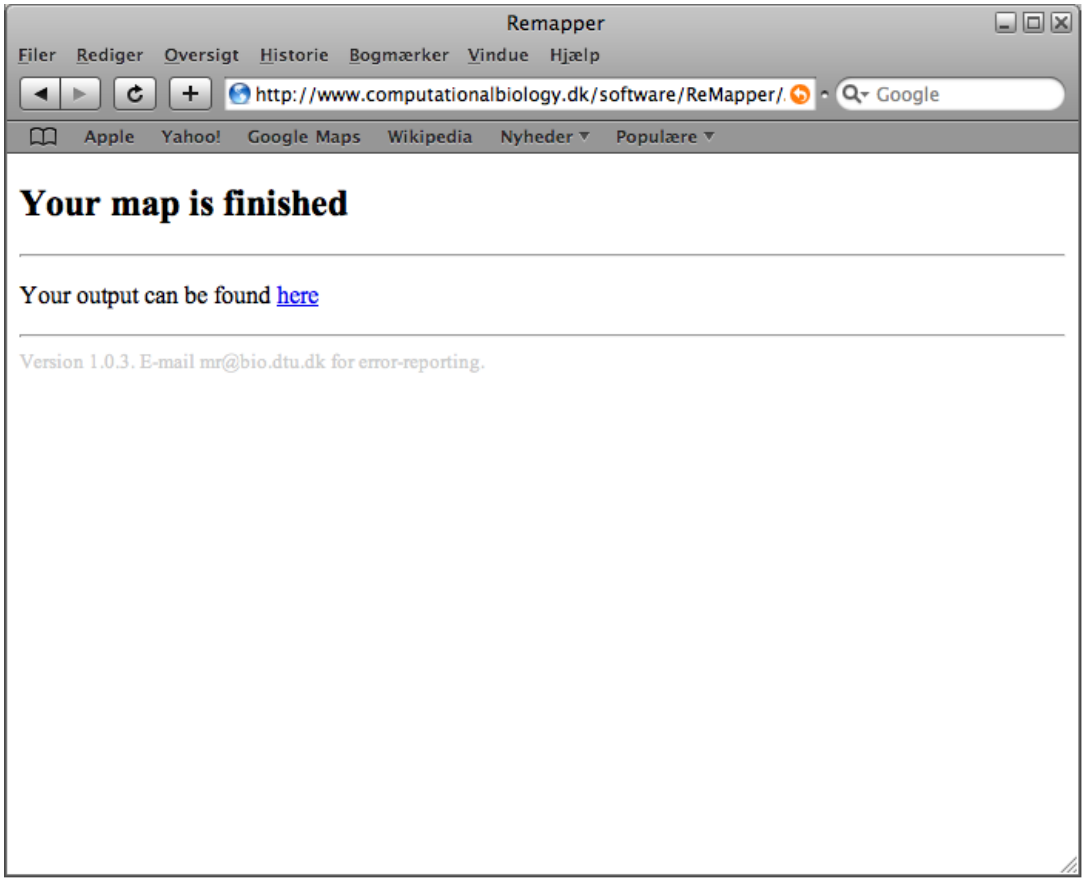


Figure B.2: ReMapper result page.

Appendix C

Supplementaries for chapter 5

Table C.1: Distribution of probe numbers per gene. Values are calculated for each genome

No	*A. nidulans* (%)	*A. niger* (%)	*A. oryzae* (%)
0	0.4	0.7	0.3
1	0.5	0.3	<0.1
2	0.7	<0.1	<0.1
3	0.6	<0.1	<0.1
4	0.6	<0.1	<0.1
5	0.8	0.3	<0.1
6	1.0	0.2	<0.1
7	1.1	0.5	<0.1
8	1.1	0.6	0.2
9	1.3	0.9	1.2
10	2.1	1.9	2.2
11	89.7	94.5	93.8

Appendix D

Supplementaries for chapter 6

Table D.1: Location and sequence of motif A in the promoter of *A. nidulans, A. niger,* and *A. oryzae* genes significantly up-regulated on xylose medium.

ORF	Location	Orientation	Sequence
JGI55668	-772	1	GGCTAAA
AO090001000069	-736	1	GGATAAA
AO090001000069	-668	-1	TTTAACC
AN0250	-491	-1	TTTACCC
AO090001000069	-342	1	GGGTAAA
JGI55668	-334	1	GGGTAAA
AO090001000069	-295	1	GGCTAAA
JGI55668	-271	1	GGCTAAA
JGI55419	-906	1	GGCTAAA
AO090003000859	-319	-1	TTTACCC
JGI51997	-310	-1	TTTAGCC
AO090003000859	-301	-1	TTTAGCC
JGI51997	-289	-1	TTTAGCC
AO090003000859	-269	-1	TTTAGCC
AN0423	-232	-1	TTTATCC
AN0423	-216	-1	TTTAGCC
JGI51997	-205	-1	TTTAGCC
AO090003000859	-195	-1	TTTATCC
AN0423	-173	-1	TTTAGCC
AN0423	-130	-1	TTTACCC
AO090005001078	-854	1	GGCTAAA
AO090005001078	-840	-1	TTTAACC
JGI46405	-840	-1	TTTAACC
JGI46405	-335	1	GGGTAAA
AO090005001078	-318	1	GGCTAAA
AN0942	-311	1	GGATAAA

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ORF	Location	Orientation	Sequence
JGI213437	-475	1	GGATAAA
AN10169	-193	-1	TTTAACC
AO090038000426	-192	1	GGTTAAA
AN10169	-137	1	GGGTAAA
JGI177736	-124	-1	TTTACCC
AN10169	-69	-1	TTTAACC
JGI205670	-827	-1	TTTAACC
AN2359	-565	-1	TTTAGCC
AN2359	-491	1	GGCTAAA
AO090005000986	-455	1	GGCTAAA
AN2359	-245	1	GGCTAAA
AO090005000986	-153	-1	TTTATCC
AN2359	-121	-1	TTTATCC
JGI55604	-354	-1	TTTATCC
AO090012000809	-234	-1	TTTACCC
JGI212893	-915	-1	TTTATCC
JGI212893	-855	-1	TTTACCC
AN3368	-632	-1	TTTATCC
AN3368	-244	1	GGGTAAA
AN3368	-112	1	GGATAAA
JGI56084	-577	-1	TTTAACC
JGI56084	-359	-1	TTTAGCC
JGI56084	-297	-1	TTTAACC
AN3432	-255	-1	TTTAGCC
AO090020000042	-224	1	GGTTAAA
AN3432	-206	-1	TTTAACC
AN3432	-174	1	GGATAAA
AO090009000275	-915	-1	TTTAGCC
AN4148	-685	1	GGATAAA
AO090011000483	-910	1	GGATAAA
JGI180923	-884	1	GGCTAAA
AO090011000483	-602	1	GGCTAAA
JGI55928	-757	-1	TTTAACC
AN7193	-584	-1	TTTAACC
AO090023000264	-321	1	GGGTAAA
AN7193	-287	1	GGGTAAA

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ORF	Location	Orientation	Sequence
JGI55928	-215	1	GGGTAAA
AN7610	-964	1	GGGTAAA
AO090012000267	-617	1	GGCTAAA
JGI212736	-996	1	GGGTAAA
JGI212736	-86	1	GGATAAA
JGI199510	-784	-1	TTTACCC
AO090020000324	-253	-1	TTTAACC
JGI209771	-831	-1	TTTATCC
AO090020000603	-781	1	GGATAAA
AO090020000603	-647	1	GGGTAAA
AO090020000603	-638	1	GGGTAAA
AN8790	-576	1	GGTTAAA
AO090020000603	-359	1	GGATAAA
JGI209771	-332	-1	TTTAGCC
AN8790	-284	1	GGATAAA
AO090020000603	-218	-1	TTTATCC
JGI209771	-142	1	GGGTAAA
AO090038000631	-723	1	GGTTAAA
AO090038000631	-632	1	GGGTAAA
AO090038000631	-436	1	GGTTAAA
AO090038000631	-414	1	GGTTAAA
AN9064	-308	1	GGATAAA
AN9064	-273	1	GGTTAAA
JGI203198	-184	1	GGGTAAA
AN9173	-903	1	GGTTAAA
AO090010000063	-755	-1	TTTAGCC
AN9173	-524	-1	TTTAGCC
JGI194438	-406	1	GGTTAAA
AO090010000063	-98	1	GGTTAAA
AN9286	-285	1	GGCTAAA
JGI56619	-270	1	GGCTAAA
AO090026000127	-259	1	GGCTAAA
JGI56619	-176	-1	TTTACCC
AO090026000127	-141	-1	TTTACCC
AN9287	-931	-1	TTTACCC
JGI54859	-255	-1	TTTAGCC
AO090701000345	-194	-1	TTTAGCC
AO090701000345	-185	-1	TTTAGCC

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ORF	Location	Orientation	Sequence
AN9287	-152	-1	TTTAGCC

Location is relative to the start-codon. Genes are sorted into homologues.

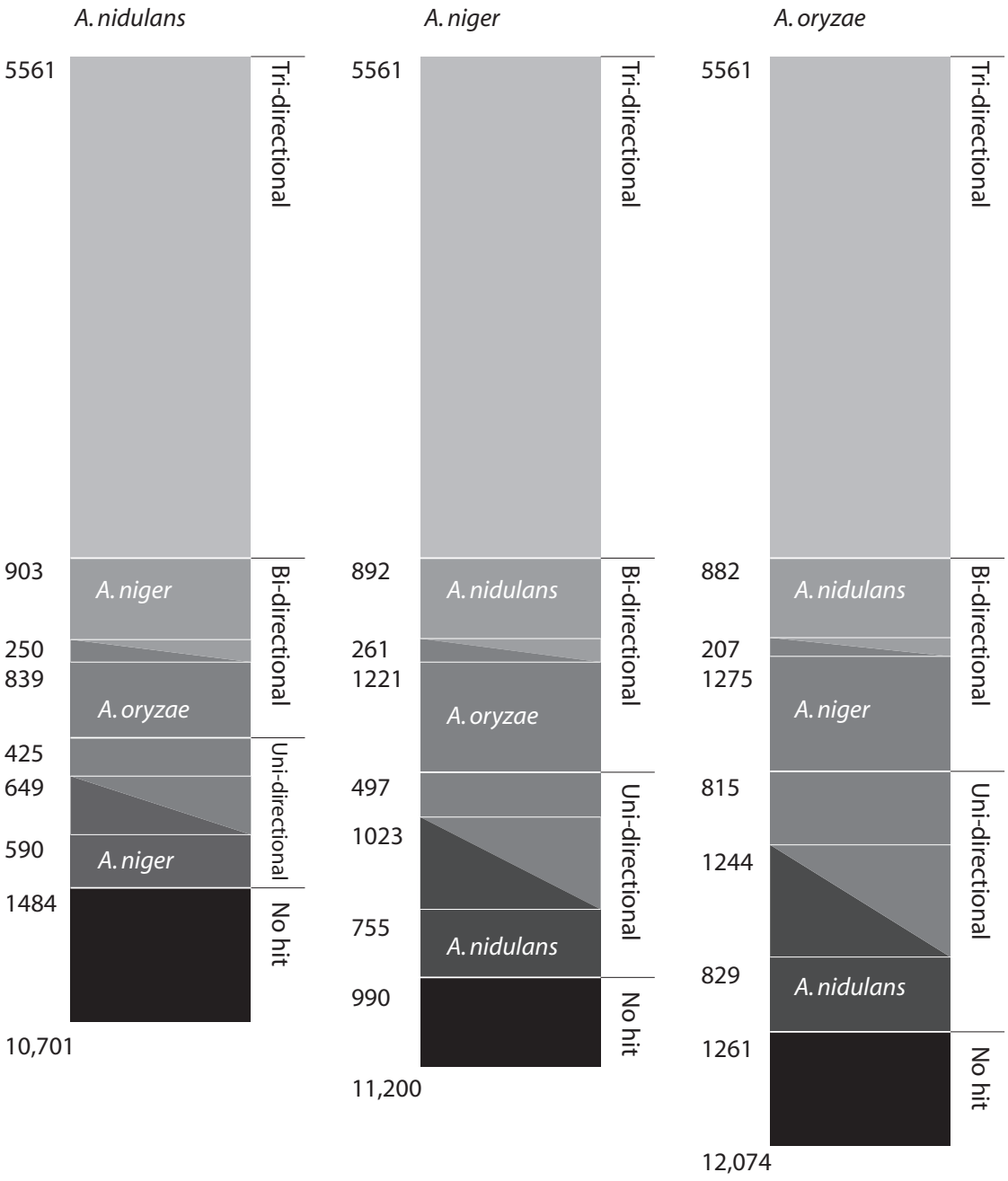

Figure D.1: The three bars show the distribution of protein sequences from three *Aspergillus* species into four categories based on blastp-comparisons. "No hit" are proteins that did not have a significant homologous protein in one of the other species. "Uni-directional" proteins have a best hit in one or both of the other species, but these hits did not have the uni-directional protein as their best hit. "Bi-directional" proteins have a best hit in one or both of the two other species, and one of these best hits had the bi-directional protein as their best hit as well. However, these two bi-directional proteins did not have the same best hit in the third species. "Tri-directional" proteins have a best hit in both of the two other species and these best hits have the other two proteins as their best hit. Sections with two shadings are proteins with hits in both of the other two species.

Table D.2: Summary of transcription data analysis for genes with known regulation by XlnR (*A. niger* and *A. oryzae*) or known regulation on xylose (*A. nidulans*).

Sign. regul.	**Trid. hit**	**Gene ID**	**Gene name**	**log2-ratio**	**Adjusted** P
Ng	N	JGI52071	xylanase-B (*xlnB/xynB*)	-5.13	8.23E-06
NgO	Y	JGI55136	1,4-β-D-arabinoxylan arabinofuranohydrolase (*axhA*)	-1.18	2.16E-03
Ng	Y	JGI211551	acetyl xylan esterase (*axeA*)	-0.67	7.72E-03
Ng	N	JGI51662	ferulic acid esterase A (*faeA*)	-6.90	1.44E-06
Ng	N	JGI211053	endoglucanase A (*eglA*)	-4.54	1.43E-04
NgO	Y	JGI51764	β-galactosidase (*lacA*)	-3.17	1.08E-03
Ng	Y	JGI207264	α-galactosidase (*aglB*)	-1.47	2.22E-02
Ng	Y	JGI53159	1,4-β-D-glucan cellobiohydrolase A (*cbhA*)	-0.62	4.09E-03
NdNgO	Y	JGI51997	D-xylose reductase (*xyrA*)	-8.45	3.52E-06
NdNgO	Y	JGI205670	β-xylosidase (*xlnD*)	-7.80	1.44E-06
NdNgO	Y	JGI56619	α-glucuronidase (*aguA*)	-5.12	1.58E-06
NdNgO	Y	JGI209771	D-xylulokinase (*xkiA*)	-5.31	1.44E-06
	N	JGI209376	Endoglucanase B (*eglB*)	-0.29	1.41E-01
	N	JGI206333	Endoglucanase C (*eglC*)	-0.14	4.19E-01
	N	JGI51773	1,4-β-D-glucan cellobiohydrolase B (*cbhB*)	0.37	9.73E-02
NdNgO	Y	AO090005000986	β-xylosidase (*xylA*)	-6.03356	8.11E-06
O	N	AO090103000423	Endoxylanase F1 (*xynF1*)	-1.24	2.84E-03
O	N	AO090001000111	Endoxylanase G1 (*xynG1*)	-0.82	3.68E-03
O	N	AO090120000026	Endoxylanase G2 (*xynG2*)	-4.14	1.85E-05
	N	AO090026000102	Endoglucanase A (*celA*)	0.03	8.94E-01
	N	AO090010000314	Endoglucanase B (*celB*)	-0.56	1.78E-01
	N	AO090001000348	Cellobiohydrolase C (*celC*)	-0.34	2.38E-01
	N	AO090012000941	Cellobiohydrolase C (*celD*)	0.08	6.87E-01
	N	AN3613	Xylanase X22 (*xlnA*)	-2.00	1.75E-01
	N	AN9365	Xylanase X24 (*xlnB*)	-4.86	5.27E-02

The first columns show which of the species have significant regulation of the gene and tri-directional best hit (if such exist). Nd, Ng and O are *A. nidulans*, *A. niger* and *A. oryzae* respectively. The column “Trid. hit” shows if the given gene has tri-directional best hits. A negative log2-ratio represents an up-regulation on xylose relative to glucose. A positive value represents up-regulation on glucose.

Table D.3: Conservation analysis of *A. fumigatus* genes. Columns 1–3 show 23 genes that are differentially expressed and conserved in *A. nidulans*, *A. niger*, and *A. oryzae*.

A. nidulans	*A. oryzae*	*A. niger*	*A. fumigatus*	*A. niger* **annotation**	**Regulation**	**Motif A**
AN0250	AO090001000069	JGI55668	N/A	Sugar transporter	Up	NdNgO
AN0280	AO090005000767	JGI55419	Afu1g03140	Glucosyl hydrolase	Up	
AN0423	AO090003000859	JGI51997	Afu1g04820	D-xylose reductase (xyrA)	Up	NdNgOFu
AN0942	AO090005001078	JGI46405	Afu1g16270	L-arabitol dehydrogenase	Up	NdNgOFu
AN10124	AO090003000497	JGI213437	Afu1g14710	β-glycosidase	Up	NgFu
AN10169	AO090038000426	JGI177736	Afu1g10100	Short-chain dehydrogenase	Up	NdNgO
AN1677	AO090023000688	JGI54541	Afu4g08710	Short-chain dehydrogenase	Up	Fu
AN2359	AO090005000986	JGI205670	Afu1g16920	β-xylosidase	Up	NdNgO
AN3184	AO090012000809	JGI55604	Afu3g13240	Aldose 1-epimerase	Up	Ng
AN3368	AO090010000208	JGI212893	Afu7g01320	Glycoside hydrolase	Up	NdNg
AN3432	AO090020000042	JGI56084	Afu3g05740	Aldose 1-epimerase	Up	NdNgOFu
AN4148	AO090009000275	JGI205766	Afu4g13080	Sugar transporter	Up	NgO
AN4590	AO090011000483	JGI180923	Afu2g02110	Sugar transporter	Up	NgO
AN5860	AO090026000494	JGI197162	Afu2g11520	Monosugar-transporter (mstC)	Down	
AN7193	AO090023000264	JGI55928	Afu6g10260	Aldo/keto reductase	Up	NdNgO
AN7610	AO090012000267	JGI48811	Afu2g15620	xlnR	Up	NgOFu
AN8138	AO090010000684	JGI212736	Afu8g01130	α-galactosidase	Up	NgFu
AN8400	AO090020000324	JGI199510	Afu3g06730	Sugar transporter	Up	NgO
AN8790	AO090020000603	JGI209771	Afu5g09840	D-xylulokinase (xkiA)	Up	NdNgOFu
AN9064	AO090038000631	JGI203198	Afu7g02550	Xylitol dehydrogenase (xdhA)	Up	NdNgOFu
AN9173	AO090010000063	JGI194438	Afu8g00890	Sugar transporter	Up	NdNgOFu
AN9286	AO090026000127	JGI56619	Afu5g14380	α-glucuronidase (aguA)	Up	NdNgOFu
AN9287	AO090701000345	JGI54859	Afu2g00820	Lipolytic enzyme	Up	NdNgOFu

The *A. fumigatus* column shows the ORF that was the best blast hit for the genes from all of the other three Aspergilli. Genes marked with "Up" are up-regulated in *A. nidulans*, *A. niger*, and *A. oryzae* when grown on xylose medium. The presence of motif A (5'-GGNTAAA-3') in the promoter region of the *A. fumigatus*, *A. nidulans*, *A. niger*, and *A. oryzae* genes is marked with Fu, Nd, Ng and O respectively.

Appendix E

Supplementaries for chapter 7

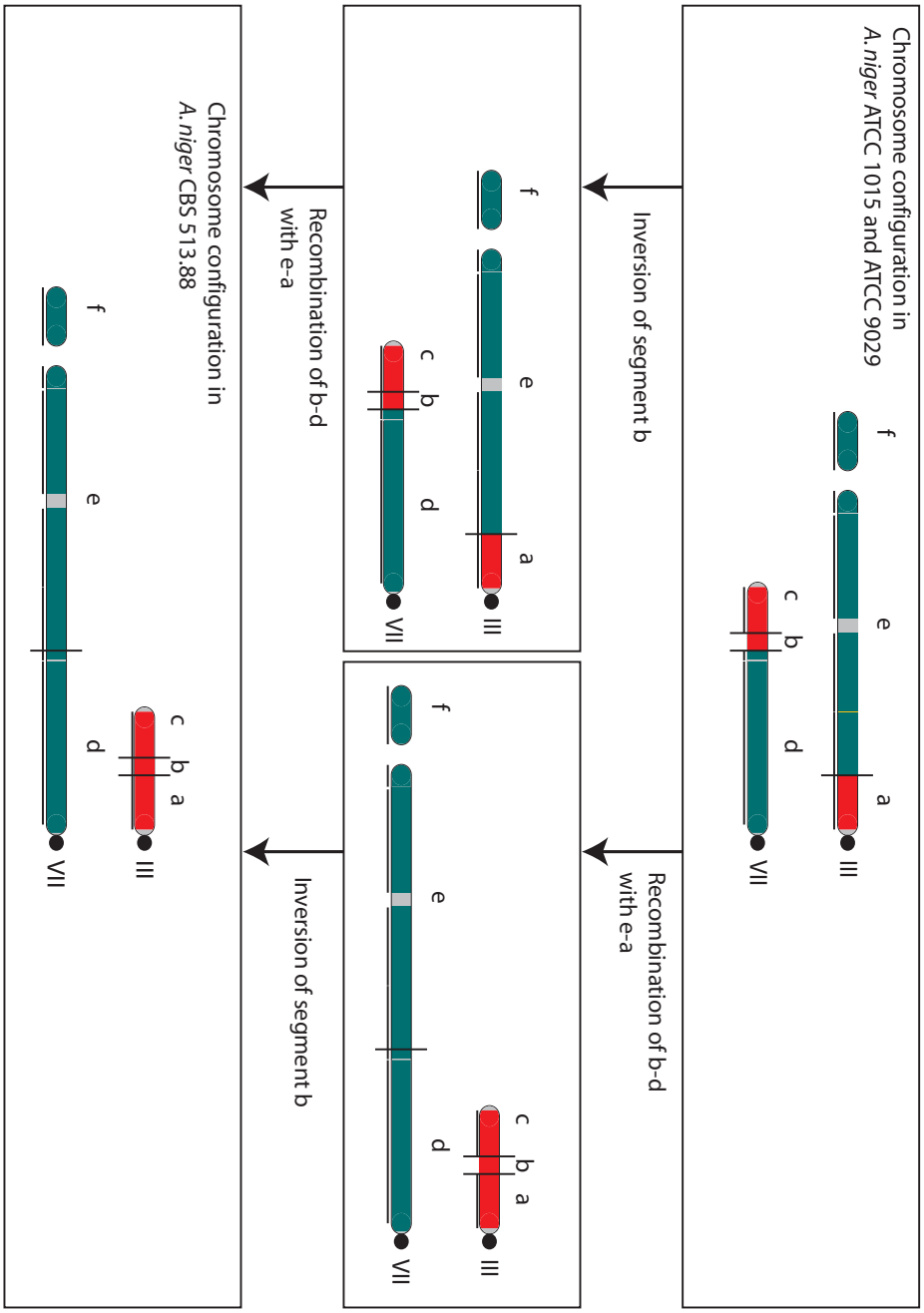

Figure E.1: Proposed set of chromosomal rearrangements leading to the genomic differences between *A. niger* CBS 513.88 and strains ATCC 1015 and ATCC 9029. Both routes are equally probable. The coloring of the chromosome arms show syntenic regions between *A. niger* CBS 513.88 and ATCC 1015 (See Figure 7.1 for details). Proposed locations of centromeric regions are shown with filled black circles. Black lines underneath the contigs denote inverted sequence relative to *A. niger* CBS 513.88. Gaps between contigs and centromeres are not to scale. Roman numerals indicate chromosome numbers.

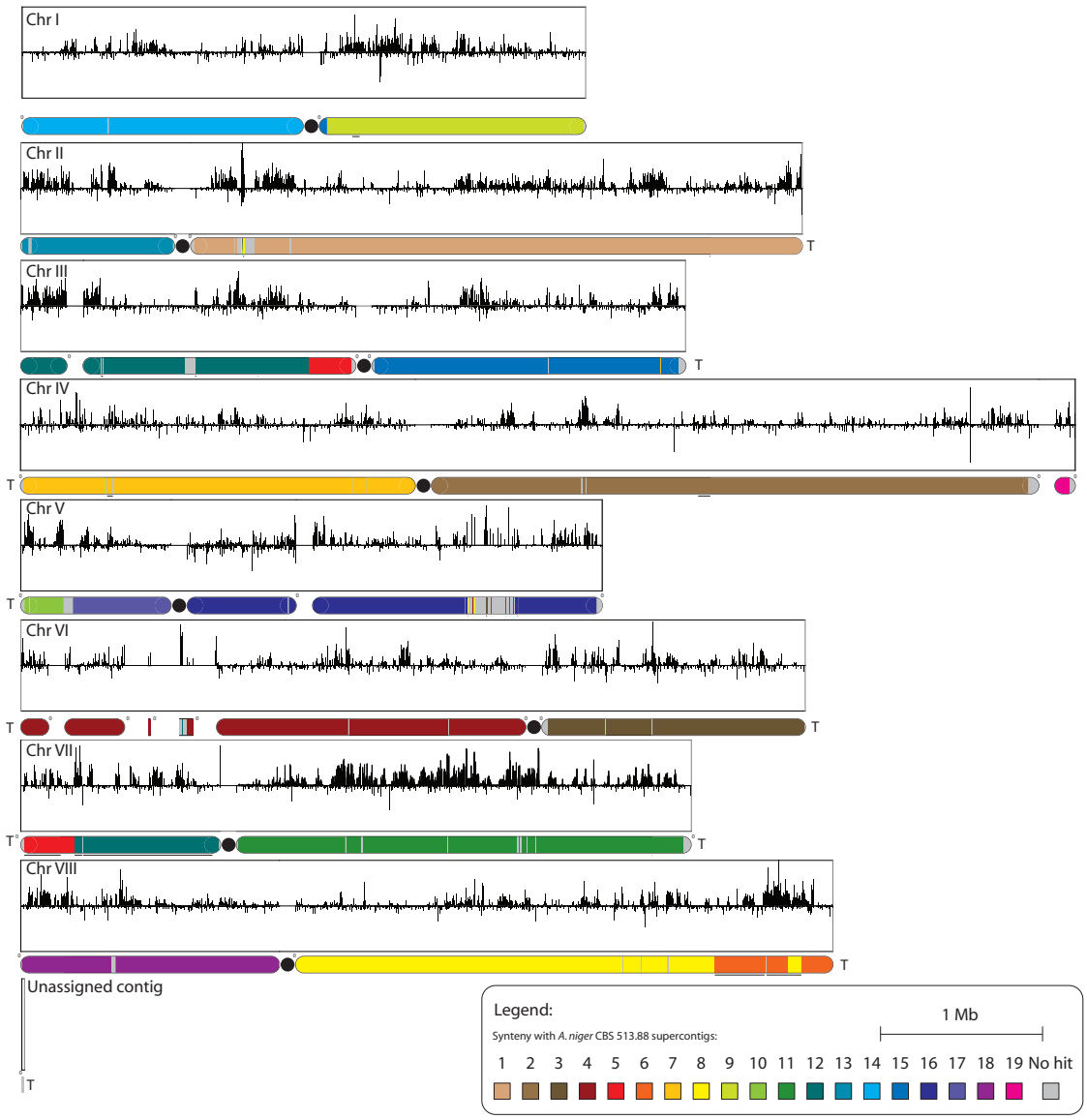

Figure E.2: Synteny map of the contigs of *A. niger* ATCC 1015 to the supercontigs of *A. niger* CBS 513.88. Colored bars show syntenic regions in *A. niger* CBS 513.88. Proposed locations of centromeric regions are shown with filled black circles. Sequenced telomeres are marked with a T. Zeroes mark the first base of the contigs. Black line underneath the contigs denote inverted sequence. Black bars shown SNPs/kb between the sequences of *A. niger* ATCC 1015 and CBS 513.88 (upper half) and *A. niger* ATCC 1015 and ATCC 9029 (lower half) (Y-axis: 0–160 SNPs/kb for both halves).

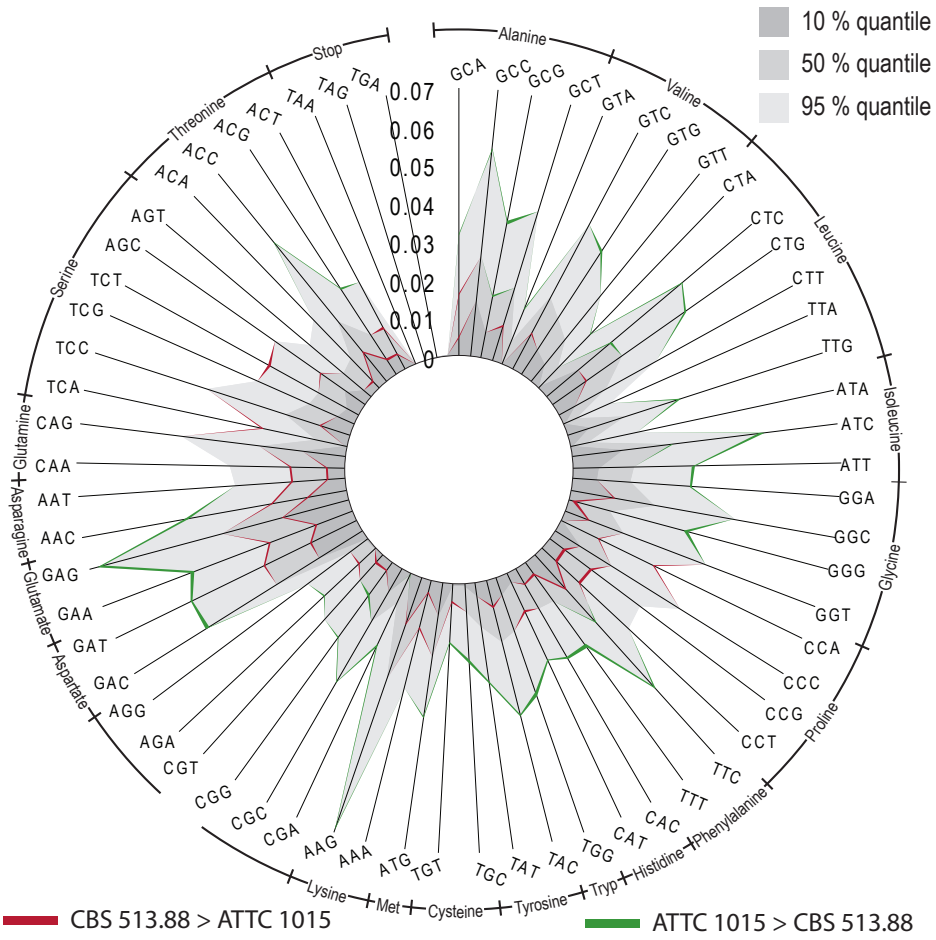

Figure E.3: Plot of codon usage analysis of 9,901 genes predicted in both ATCC 1015, and CBS 513.88. Each colored band shows a percentile. If the band is red, the percentile of *A. niger* CBS 513.88 follows the outer rim of the band, while the percentile of ATCC 1015 follows the inner rim. A green band indicates the opposite.

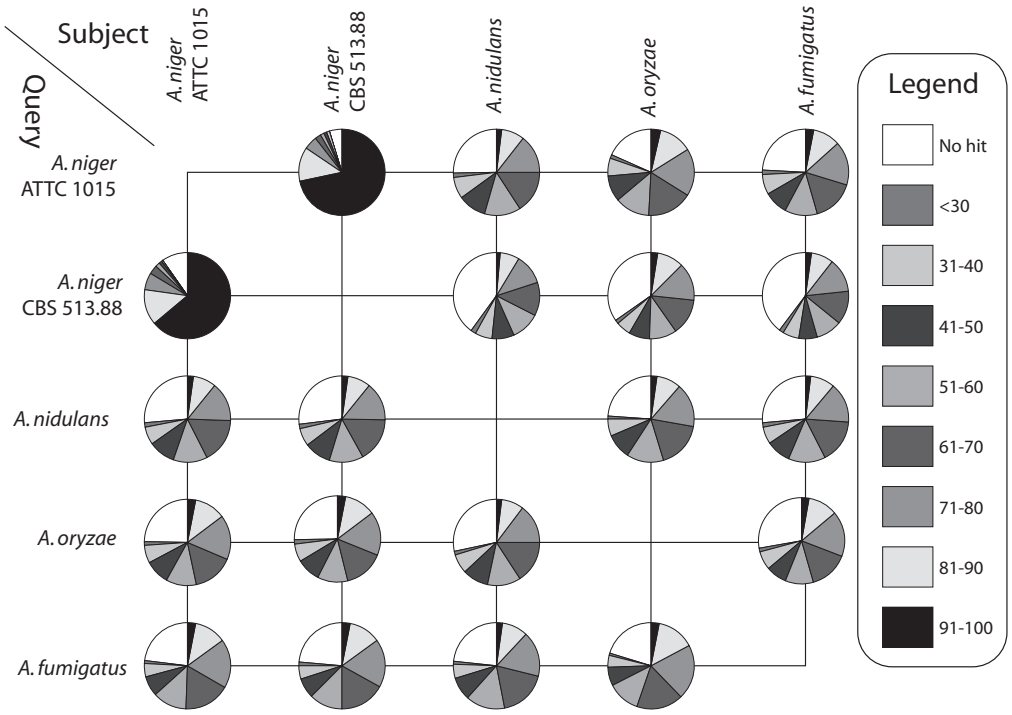

Figure E.4: Pie-chart summaries of *Aspergillus* tblastn comparisons. The predicted proteins of the query genome sequences were blasted against the nucleotide sequence of the subjects. A e-value cut-off of 1e-50 was applied. The pie-charts show the distribution of highest identity hit for each protein of the query sequence. A lower percentage of the predicted proteins of *A. niger* CBS 513.88 is conserved in the other Aspergilli than those predicted in ATCC 1015.

E.1 GO-term over-representation tables for Imprint analysis

E.1.1 Imprint category A

GO term over-representation results for category A of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############
```

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0003735	structural constituent of ribosome	134	73	36.84	2	2.5e-11	1.00	2.5e-11	1.00000
2	GO:0005525	GTP binding	94	45	25.84	3	1.7e-05	1.00	1.7e-05	1.7e-05
3	GO:0004129	cytochrome-c oxidase activity	5	5	1.37	7	0.00156	1.00	0.0016	1.00000
4	GO:0015078	hydrogen ion transporter activity	45	24	12.37	5	0.00021	0.99	0.0052	0.00021
5	GO:0003747	translation release factor activity	4	4	1.10	15	0.00570	0.89	0.0057	0.00570
6	GO:0004594	pantothenate kinase activity	4	4	1.10	16	0.00570	0.92	0.0057	0.00570
7	GO:0005199	structural constituent of cell wall	4	4	1.10	17	0.00570	0.98	0.0057	1.00000
8	GO:0000158	protein phosphatase type 2A activity	10	7	2.75	19	0.00622	0.90	0.0062	0.00622
9	GO:0004723	calcium-dependent protein serine/threoni...	10	7	2.75	20	0.00622	0.90	0.0062	0.00622
10	GO:0004724	magnesium-dependent protein serine/threo...	10	7	2.75	21	0.00622	0.90	0.0062	0.00622
11	GO:0008420	CTD phosphatase activity	10	7	2.75	22	0.00622	0.90	0.0062	0.00622
12	GO:0008597	calcium-dependent protein serine/threoni...	10	7	2.75	23	0.00622	0.90	0.0062	0.00622
13	GO:0015071	protein phosphatase type 2C activity	10	7	2.75	24	0.00622	0.90	0.0062	0.00622
14	GO:0017018	myosin phosphatase activity	10	7	2.75	25	0.00622	0.90	0.0062	0.00622
15	GO:0017020	myosin phosphatase regulator activity	10	7	2.75	26	0.00622	0.90	0.0062	0.00622
16	GO:0030357	protein phosphatase type 2B activity	10	7	2.75	27	0.00622	0.90	0.0062	0.00622
17	GO:0003880	C-terminal protein carboxyl methyltransf...	8	6	2.20	29	0.00704	0.91	0.0070	0.00704
18	GO:0009008	DNA-methyltransferase activity	8	6	2.20	30	0.00704	0.88	0.0070	0.00704
19	GO:0016418	S-acetyltransferase activity	6	5	1.65	31	0.00723	0.72	0.0072	0.00723
20	GO:0030523	dihydrolipoamide S-acyltransferase activ...	6	5	1.65	32	0.00723	0.72	0.0072	0.00723
21	GO:0046933	hydrogen ion transporting ATP synthase a...	31	15	8.52	33	0.01038	0.99	0.0104	1.00000
22	GO:0046961	hydrogen ion transporting ATPase activit...	31	15	8.52	34	0.01038	0.99	0.0104	1.00000
23	GO:0003924	GTPase activity	29	14	7.97	35	0.01345	1.00	0.0134	0.01345
24	GO:0004298	threonine endopeptidase activity	16	9	4.40	36	0.01426	0.65	0.0143	0.01426
25	GO:0000179	rRNA (adenine-N6,N6-)-dimethyltransferas...	7	5	1.92	37	0.01958	0.86	0.0196	0.01958
26	GO:0008174	mRNA methyltransferase activity	7	5	1.92	38	0.01958	0.86	0.0196	0.01958
27	GO:0008326	site-specific DNA-methyltransferase (cyt...	7	5	1.92	39	0.01958	0.86	0.0196	1.00000
28	GO:0008649	rRNA methyltransferase activity	7	5	1.92	40	0.01958	0.86	0.0196	1.00000
29	GO:0008650	rRNA (uridine-2’-O-)-methyltransferase a...	7	5	1.92	41	0.01958	0.86	0.0196	0.01958
30	GO:0009383	rRNA (cytosine-C5-967)-methyltransferase...	7	5	1.92	42	0.01958	0.86	0.0196	0.01958
31	GO:0016205	selenocysteine methyltransferase activit...	7	5	1.92	43	0.01958	0.86	0.0196	0.01958
32	GO:0016273	arginine N-methyltransferase activity	7	5	1.92	44	0.01958	0.86	0.0196	1.00000
33	GO:0016274	protein-arginine N-methyltransferase act...	7	5	1.92	45	0.01958	0.86	0.0196	0.01958
34	GO:0016300	tRNA (uracil) methyltransferase activity	7	5	1.92	46	0.01958	0.86	0.0196	0.01958
35	GO:0016424	tRNA (guanosine) methyltransferase activ...	7	5	1.92	47	0.01958	0.86	0.0196	0.01958
36	GO:0016426	tRNA (adenine)-methyltransferase activit...	7	5	1.92	48	0.01958	0.86	0.0196	0.01958
37	GO:0016427	tRNA (cytosine)-methyltransferase activi...	7	5	1.92	49	0.01958	0.86	0.0196	0.01958
38	GO:0016431	tRNA (uridine) methyltransferase activit...	7	5	1.92	50	0.01958	0.86	0.0196	0.01958
39	GO:0016433	rRNA (adenine) methyltransferase activit...	7	5	1.92	51	0.01958	0.86	0.0196	1.00000
40	GO:0016434	rRNA (cytosine) methyltransferase activi...	7	5	1.92	52	0.01958	0.86	0.0196	1.00000
41	GO:0016435	rRNA (guanine) methyltransferase activit...	7	5	1.92	53	0.01958	0.86	0.0196	0.01958

42	GO:0016436	rRNA (uridine) methyltransferase activit...	7	5	1.92	54	0.01958	0.86	0.0196	1.00000
43	GO:0018423	protein-leucine O-methyltransferase acti...	7	5	1.92	55	0.01958	0.86	0.0196	0.01958
44	GO:0018707	1-phenanthrol methyltransferase activity	7	5	1.92	56	0.01958	0.86	0.0196	0.01958
45	GO:0019702	protein-arginine N5-methyltransferase ac...	7	5	1.92	57	0.01958	0.86	0.0196	0.01958
46	GO:0030792	methylarsonite methyltransferase activit...	7	5	1.92	58	0.01958	0.86	0.0196	0.01958
47	GO:0003849	3-deoxy-7-phosphoheptulonate synthase ac...	3	3	0.82	59	0.02075	0.98	0.0207	0.02075
48	GO:0003868	4-hydroxyphenylpyruvate dioxygenase acti...	3	3	0.82	60	0.02075	0.99	0.0207	0.02075
49	GO:0004462	lactoylglutathione lyase activity	3	3	0.82	61	0.02075	0.80	0.0207	0.02075
50	GO:0004749	ribose phosphate diphosphokinase activit...	3	3	0.82	62	0.02075	1.00	0.0207	0.02075
51	GO:0004849	uridine kinase activity	3	3	0.82	63	0.02075	0.94	0.0207	0.02075
52	GO:0005338	nucleotide-sugar transporter activity	3	3	0.82	64	0.02075	1.00	0.0207	0.02075
53	GO:0008519	ammonium transporter activity	3	3	0.82	65	0.02075	1.00	0.0207	0.02075
54	GO:0015101	organic cation transporter activity	3	3	0.82	66	0.02075	1.00	0.0207	1.00000
55	GO:0019904	protein domain specific binding	3	3	0.82	67	0.02075	1.00	0.0207	0.02075
56	GO:0016811	hydrolase activity, acting on carbon-nit...	39	17	10.72	68	0.02200	0.72	0.0220	0.02200
57	GO:0003988	acetyl-CoA C-acyltransferase activity	5	4	1.37	69	0.02223	0.75	0.0222	0.02223
58	GO:0004379	glycylpeptide N-tetradecanoyltransferase...	5	4	1.37	70	0.02223	0.68	0.0222	0.02223
59	GO:0017169	CDP-alcohol phosphatidyltransferase acti...	5	4	1.37	71	0.02223	0.76	0.0222	0.02223
60	GO:0019107	myristoyltransferase activity	5	4	1.37	72	0.02223	0.68	0.0222	1.00000
61	GO:0016408	C-acyltransferase activity	12	7	3.30	73	0.02402	0.67	0.0240	0.72266
62	GO:0019205	nucleobase, nucleoside, nucleotide kinas...	12	7	3.30	74	0.02402	0.97	0.0240	1.00000
63	GO:0003743	translation initiation factor activity	26	12	7.15	77	0.03185	0.98	0.0319	0.03185
64	GO:0008135	translation factor activity, nucleic aci...	36	18	9.90	12	0.00331	0.98	0.0343	0.35343
65	GO:0045182	translation regulator activity	36	18	9.90	13	0.00331	0.98	0.0343	0.47229
66	GO:0008408	3’-5’ exonuclease activity	13	7	3.57	79	0.03990	0.81	0.0399	0.03990
67	GO:0008175	tRNA methyltransferase activity	8	5	2.20	82	0.04048	0.84	0.0405	1.00000
68	GO:0008425	2-polyprenyl-6-methoxy-1,4-benzoquinone ...	8	5	2.20	83	0.04048	0.84	0.0405	0.04048
69	GO:0016423	tRNA (guanine) methyltransferase activit...	8	5	2.20	84	0.04048	0.84	0.0405	0.04048
70	GO:0030580	quinone cofactor methyltransferase activ...	8	5	2.20	85	0.04048	0.84	0.0405	1.00000
71	GO:0019829	cation-transporting ATPase activity	39	16	10.72	86	0.04649	0.99	0.0465	0.89364

########## Cellular component #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005840	ribosome	134	73	39.39	4	3.5e-10	1.00	8.8e-09	1.0000
2	GO:0043234	protein complex	475	202	139.63	1	4.5e-12	1.00	0.0013	0.0050
3	GO:0044445	cytosolic part	5	5	1.47	14	0.0022	0.98	0.0022	0.0022
4	GO:0005732	small nucleolar ribonucleoprotein comple...	16	10	4.70	22	0.0059	0.99	0.0059	1.0000
5	GO:0005740	mitochondrial envelope	47	22	13.82	25	0.0081	0.98	0.0081	0.3855
6	GO:0015935	small ribosomal subunit	12	8	3.53	26	0.0081	1.00	0.0081	1.0000
7	GO:0005963	magnesium-dependent protein serine/threo...	10	7	2.94	27	0.0092	0.84	0.0092	0.0092
8	GO:0017023	myosin phosphatase complex	10	7	2.94	28	0.0092	0.84	0.0092	1.0000
9	GO:0016591	DNA-directed RNA polymerase II, holoenzy...	6	5	1.76	29	0.0099	0.99	0.0099	1.0000
10	GO:0031966	mitochondrial membrane	40	19	11.76	30	0.0112	0.99	0.0112	1.0000
11	GO:0005743	mitochondrial inner membrane	35	17	10.29	31	0.0124	0.99	0.0124	0.0124
12	GO:0019866	organelle inner membrane	35	17	10.29	32	0.0124	0.99	0.0124	1.0000
13	GO:0016469	proton-transporting two-sector ATPase co...	34	16	9.99	33	0.0213	0.97	0.0213	1.0000
14	GO:0005667	transcription factor complex	9	6	2.65	36	0.0226	0.91	0.0226	1.0000
15	GO:0044455	mitochondrial membrane part	7	5	2.06	37	0.0262	0.97	0.0262	0.0262
16	GO:0005773	vacuole	5	4	1.47	38	0.0284	1.00	0.0284	0.5003
17	GO:0031090	organelle membrane	88	34	25.87	39	0.0366	0.93	0.0366	0.4783
18	GO:0000785	chromatin	23	11	6.76	41	0.0468	0.59	0.0468	0.0468

########## Biological process #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0006412	translation	231	109	65.25	1	2.8e-10	1.00	2.2e-09	2.2e-09
2	GO:0007264	small GTPase mediated signal transductio...	40	26	11.30	3	1.3e-06	0.98	1.3e-06	1.3e-06
3	GO:0008654	phospholipid biosynthetic process	20	13	5.65	11	0.00066	0.91	0.00066	0.0022
4	GO:0015031	protein transport	107	46	30.22	13	0.00067	0.99	0.00067	0.3062
5	GO:0022613	ribonucleoprotein complex biogenesis and...	36	18	10.17	23	0.00453	0.96	0.00453	0.3148
6	GO:0006397	mRNA processing	26	14	7.34	25	0.00515	0.99	0.00515	0.0052
7	GO:0009116	nucleoside metabolic process	19	11	5.37	27	0.00634	0.94	0.00634	0.0352
8	GO:0006415	translational termination	4	4	1.13	28	0.00634	0.87	0.00634	1.0000
9	GO:0030041	actin filament polymerization	4	4	1.13	29	0.00634	1.00	0.00634	0.0063
10	GO:0065004	protein-DNA complex assembly	24	13	6.78	34	0.00654	0.95	0.00654	0.0587
11	GO:0015986	ATP synthesis coupled proton transport	32	16	9.04	35	0.00731	0.99	0.00731	0.0073
12	GO:0006366	transcription from RNA polymerase II pro...	6	5	1.69	41	0.00821	1.00	0.00821	0.0082
13	GO:0046164	alcohol catabolic process	30	15	8.47	42	0.00930	0.96	0.00930	1.0000
14	GO:0006007	glucose catabolic process	28	14	7.91	43	0.01186	0.96	0.01186	0.0119
15	GO:0019320	hexose catabolic process	28	14	7.91	44	0.01186	0.96	0.01186	0.4834
16	GO:0046365	monosaccharide catabolic process	28	14	7.91	45	0.01186	0.96	0.01186	1.0000
17	GO:0009057	macromolecule catabolic process	79	32	22.31	46	0.01207	1.00	0.01207	0.6276
18	GO:0042254	ribosome biogenesis and assembly	11	7	3.11	55	0.01526	0.92	0.01526	0.0153
19	GO:0044265	cellular macromolecule catabolic process	66	27	18.64	58	0.01751	0.92	0.01751	1.0000
20	GO:0006769	nicotinamide metabolic process	14	8	3.95	61	0.02178	0.98	0.02178	1.0000
21	GO:0019362	pyridine nucleotide metabolic process	14	8	3.95	62	0.02178	0.98	0.02178	1.0000
22	GO:0006766	vitamin metabolic process	27	13	7.63	63	0.02182	0.99	0.02182	1.0000
23	GO:0006767	water-soluble vitamin metabolic process	27	13	7.63	64	0.02182	0.99	0.02182	1.0000
24	GO:0000103	sulfate assimilation	3	3	0.85	65	0.02250	1.00	0.02250	0.0225
25	GO:0006791	sulfur utilization	3	3	0.85	66	0.02250	1.00	0.02250	1.0000
26	GO:0008064	regulation of actin polymerization and/o...	3	3	0.85	67	0.02250	0.99	0.02250	1.0000
27	GO:0009132	nucleoside diphosphate metabolic process	3	3	0.85	68	0.02250	0.85	0.02250	1.0000
28	GO:0009186	deoxyribonucleoside diphosphate metaboli...	3	3	0.85	69	0.02250	0.85	0.02250	0.2821
29	GO:0009221	pyrimidine deoxyribonucleotide biosynthe...	3	3	0.85	70	0.02250	0.85	0.02250	1.0000
30	GO:0009263	deoxyribonucleotide biosynthetic process	3	3	0.85	71	0.02250	0.85	0.02250	1.0000
31	GO:0015780	nucleotide-sugar transport	3	3	0.85	72	0.02250	1.00	0.02250	0.0225
32	GO:0030832	regulation of actin filament length	3	3	0.85	73	0.02250	0.99	0.02250	1.0000
33	GO:0030833	regulation of actin filament polymerizat...	3	3	0.85	74	0.02250	0.99	0.02250	1.0000
34	GO:0051128	regulation of cell organization and biog...	3	3	0.85	75	0.02250	0.99	0.02250	1.0000
35	GO:0016052	carbohydrate catabolic process	30	14	8.47	77	0.02390	0.96	0.02390	1.0000
36	GO:0044275	cellular carbohydrate catabolic process	30	14	8.47	78	0.02390	0.96	0.02390	1.0000
37	GO:0009117	nucleotide metabolic process	85	38	24.01	16	0.00079	0.93	0.02391	0.9475
38	GO:0006464	protein modification	368	121	103.94	79	0.02395	1.00	0.02395	0.0790
39	GO:0006213	pyrimidine nucleoside metabolic process	5	4	1.41	80	0.02457	0.77	0.02457	1.0000
40	GO:0006364	rRNA processing	5	4	1.41	81	0.02457	0.96	0.02457	1.0000
41	GO:0006367	transcription initiation from RNA polyme...	5	4	1.41	82	0.02457	0.99	0.02457	1.0000
42	GO:0009219	pyrimidine deoxyribonucleotide metabolic...	5	4	1.41	83	0.02457	0.77	0.02457	0.4845
43	GO:0016072	rRNA metabolic process	5	4	1.41	84	0.02457	0.96	0.02457	1.0000
44	GO:0006996	organelle organization and biogenesis	96	39	27.12	26	0.00562	0.97	0.02466	0.8323
45	GO:0006733	oxidoreduction coenzyme metabolic proces...	17	9	4.80	86	0.02737	0.98	0.02737	1.0000
46	GO:0006352	transcription initiation	12	7	3.39	87	0.02780	0.96	0.02780	1.0000
47	GO:0006732	coenzyme metabolic process	95	41	26.83	17	0.00119	0.99	0.03028	0.8566
48	GO:0006006	glucose metabolic process	31	14	8.76	89	0.03254	0.96	0.03254	0.8083
49	GO:0007001	chromosome organization and biogenesis (...	35	15	9.89	93	0.04475	0.97	0.04475	0.2218
50	GO:0006098	pentose-phosphate shunt	8	5	2.26	94	0.04523	0.99	0.04523	1.0000

```
51  GO:0006739                     NADP metabolic process         8           5     2.26              95 0.04523 0.99 0.04523  1.0000
52  GO:0006740                        NADPH regeneration          8           5     2.26              96 0.04523 0.99 0.04523  1.0000
53  GO:0009262       deoxyribonucleotide metabolic process         8           5     2.26              97 0.04523 0.55 0.04523  1.0000
54  GO:0006092 main pathways of carbohydrate metabolic ...        59          23    16.66              99 0.04774 0.92 0.04774  0.5949
55  GO:0043412                     biopolymer modification       394         126   111.29             100 0.04932 0.89 0.04932  0.6457
```

E.1.2 Imprint category B

GO term over-representation results for category B of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1  GO:0003735          structural constituent of ribosome       134          38    20.86               1 0.00010 1.00 0.00010 0.00010
2  GO:0004815              aspartate-tRNA ligase activity         8           6     1.25               3 0.00030 1.00 0.00030 0.00030
3  GO:0008320                    protein carrier activity         4           4     0.62               4 0.00058 0.99 0.00058 0.00058
4  GO:0003899        DNA-directed RNA polymerase activity        33          13     5.14               5 0.00079 0.90 0.00079 0.00079
5  GO:0004100                    chitin synthase activity         6           4     0.93              11 0.00673 0.91 0.00673 0.00673
6  GO:0003994                aconitate hydratase activity         4           3     0.62              12 0.01330 1.00 0.01330 0.01330
7  GO:0016840              carbon-nitrogen lyase activity         7           4     1.09              13 0.01378 1.00 0.01378 1.00000
8  GO:0003779                              actin binding        19           7     2.96              15 0.01964 0.82 0.01964 0.01964
9  GO:0004816             asparagine-tRNA ligase activity         2           2     0.31              16 0.02422 1.00 0.02422 0.02422
10 GO:0004824                 lysine-tRNA ligase activity         2           2     0.31              17 0.02422 0.98 0.02422 0.02422
11 GO:0016842                     amidine-lyase activity         2           2     0.31              18 0.02422 1.00 0.02422 0.02422
12 GO:0018024 histone-lysine N-methyltransferase activ...        2           2     0.31              19 0.02422 0.98 0.02422 0.02422
13 GO:0042054          histone methyltransferase activity         2           2     0.31              20 0.02422 0.98 0.02422 1.00000
14 GO:0008092                cytoskeletal protein binding        20           7     3.11              21 0.02627 0.81 0.02627 0.39691
15 GO:0016810 hydrolase activity, acting on carbon-nit...        95          22    14.79              24 0.03240 0.83 0.03240 0.58638
16 GO:0016667 oxidoreductase activity, acting on sulfu...        9           4     1.40              25 0.03828 0.83 0.03828 1.00000
17 GO:0008565                protein transporter activity        80          22    12.46              10 0.00426 0.57 0.03945 0.03945
18 GO:0003723                                 RNA binding        76          18    11.83              26 0.04079 0.63 0.04079 0.04079
19 GO:0004713            protein-tyrosine kinase activity       119          26    18.53              27 0.04171 0.67 0.04171 0.03042
20 GO:0008415                    acyltransferase activity       109          24    16.97              30 0.04526 0.72 0.04526 0.72699
21 GO:0004022              alcohol dehydrogenase activity        18           6     2.80              31 0.04885 0.47 0.04885 0.04885
22 GO:0004316 3-oxoacyl-[acyl-carrier-protein] reducta...        18           6     2.80              32 0.04885 0.86 0.04885 0.04885

##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1  GO:0005737                                cytoplasm       418         116    72.25               1 1.9e-09 1.00 1.2e-05 3.3e-09
2  GO:0005840                                ribosome        134          38    23.16              10 0.00071 1.00  0.0007  0.3945
3  GO:0005643                              nuclear pore        15           7     2.59              13 0.00791 0.52  0.0079  0.0079
4  GO:0005740                   mitochondrial envelope        47          15     8.12              18 0.00983 0.71  0.0098  0.6731
5  GO:0005739                             mitochondrion        71          24    12.27               6 0.00047 0.96  0.0128  1.0000
6  GO:0031966                   mitochondrial membrane        40          13     6.91              20 0.01348 0.71  0.0135  0.4292
7  GO:0005743          mitochondrial inner membrane        35          11     6.05              22 0.02865 0.56  0.0286  0.5275
8  GO:0019866              organelle inner membrane        35          11     6.05              23 0.02865 0.56  0.0286  0.4302
9  GO:0015934                large ribosomal subunit         8           4     1.38              24 0.03442 0.97  0.0344  1.0000
10 GO:0044422                       organelle part       242          61    41.83               8 0.00063 0.28  0.0455  0.9490
11 GO:0044446          intracellular organelle part       242          61    41.83               9 0.00063 0.28  0.0455  0.9619
```

```
##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1  GO:0006412                              translation       231          61    35.71               2 7.6e-06 1.00 8.3e-05 0.00011
2  GO:0006422            aspartyl-tRNA aminoacylation         7           5     1.08              14 0.00139 1.00  0.0014 0.00139
3  GO:0000059     protein import into nucleus, docking        10           6     1.55              16 0.00161 1.00  0.0016 0.00161
4  GO:0006094                          gluconeogenesis         3           3     0.46              26 0.00368 1.00  0.0037 0.00368
5  GO:0000096       sulfur amino acid metabolic process        12           6     1.86              28 0.00535 0.84  0.0054 0.01110
6  GO:0006807       nitrogen compound metabolic process       262          63    40.50               5 0.00012 0.79  0.0056 0.63124
7  GO:0000271       polysaccharide biosynthetic process         9           5     1.39              29 0.00638 0.96  0.0064 1.00000
8  GO:0042775 ATP synthesis coupled electron transport...         9           5     1.39              30 0.00638 0.99  0.0064 0.00638
9  GO:0046907                   intracellular transport       110          31    17.01              10 0.00041 0.90  0.0076 0.01828
10 GO:0000097     sulfur amino acid biosynthetic process         7           4     1.08              35 0.01342 0.95  0.0134 1.00000
11 GO:0006996      organelle organization and biogenesis        96          23    14.84              37 0.01828 0.95  0.0183 0.66676
12 GO:0009056                       catabolic process       144          32    22.26              38 0.01847 0.99  0.0185 0.96886
13 GO:0006099                 tricarboxylic acid cycle        15           6     2.32              41 0.01919 1.00  0.0192 0.01919
14 GO:0009060                      aerobic respiration        15           6     2.32              42 0.01919 1.00  0.0192 1.00000
15 GO:0009109                coenzyme catabolic process        15           6     2.32              43 0.01919 1.00  0.0192 1.00000
16 GO:0045333                      cellular respiration        15           6     2.32              44 0.01919 1.00  0.0192 1.00000
17 GO:0046356              acetyl-CoA catabolic process        15           6     2.32              45 0.01919 1.00  0.0192 1.00000
18 GO:0051187                cofactor catabolic process        15           6     2.32              46 0.01919 1.00  0.0192 1.00000
19 GO:0006555              methionine metabolic process         8           4     1.24              49 0.02359 0.97  0.0236 1.00000
20 GO:0006421          asparaginyl-tRNA aminoacylation         2           2     0.31              51 0.02387 1.00  0.0239 0.02387
21 GO:0006430               lysyl-tRNA aminoacylation         2           2     0.31              52 0.02387 0.98  0.0239 0.02387
22 GO:0006885                         regulation of pH         2           2     0.31              53 0.02387 0.97  0.0239 0.02387
23 GO:0042546           cell wall biosynthetic process         2           2     0.31              54 0.02387 1.00  0.0239 0.15441
24 GO:0048878                     chemical homeostasis         2           2     0.31              55 0.02387 0.97  0.0239 1.00000
25 GO:0050801                         ion homeostasis         2           2     0.31              56 0.02387 0.97  0.0239 1.00000
26 GO:0009308                  amine metabolic process       236          55    36.48              13 0.00075 0.72  0.0259 0.85754
27 GO:0006031              chitin biosynthetic process         5           3     0.77              60 0.02883 0.88  0.0288 1.00000
28 GO:0006042         glucosamine biosynthetic process         5           3     0.77              61 0.02883 0.88  0.0288 1.00000
29 GO:0006045 N-acetylglucosamine biosynthetic process         5           3     0.77              62 0.02883 0.88  0.0288 1.00000
30 GO:0009086          methionine biosynthetic process         5           3     0.77              63 0.02883 1.00  0.0288 1.00000
31 GO:0046349         amino sugar biosynthetic process         5           3     0.77              64 0.02883 0.88  0.0288 1.00000
32 GO:0043284          biopolymer biosynthetic process        18           9     2.78              12 0.00063 0.95  0.0367 0.00206
33 GO:0006414                 translational elongation         9           4     1.39              73 0.03736 0.97  0.0374 1.00000
34 GO:0006399                   tRNA metabolic process        68          20    10.51              21 0.00245 0.98  0.0394 0.26871
35 GO:0044248                cellular catabolic process       131          28    20.25              75 0.04190 0.98  0.0419 0.96366
36 GO:0006886            intracellular protein transport        82          23    12.68              20 0.00239 1.00  0.0421 0.62927
37 GO:0006520               amino acid metabolic process       221          51    34.16              15 0.00147 0.82  0.0457 0.89469
38 GO:0006084               acetyl-CoA metabolic process        18           6     2.78              77 0.04733 1.00  0.0473 1.00000
39 GO:0007010 cytoskeleton organization and biogenesis        32           9     4.95              78 0.04821 0.97  0.0482 0.32295
```

E.1.3 Imprint categories A and B combined

GO term over-representation results for category A+B of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############
```

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0003735	structural constituent of ribosome	134	111	57.70	2	1.0e-21	1.00	1.0e-21	1.0000
2	GO:0005525	GTP binding	94	63	40.48	3	2.0e-06	1.00	2.0e-06	2.0e-06
3	GO:0003899	DNA-directed RNA polymerase activity	33	24	14.21	8	0.00052	0.94	0.00052	0.1840
4	GO:0015078	hydrogen ion transporter activity	45	33	19.38	6	3.5e-05	1.00	0.00129	0.3932
5	GO:0004298	threonine endopeptidase activity	16	13	6.89	11	0.00211	0.66	0.00211	0.0021
6	GO:0008135	translation factor activity, nucleic aci...	36	24	15.50	12	0.00356	0.99	0.00356	0.0205
7	GO:0004721	phosphoprotein phosphatase activity	31	21	13.35	14	0.00476	0.98	0.00476	0.1992
8	GO:0046933	hydrogen ion transporting ATP synthase a...	31	21	13.35	15	0.00476	1.00	0.00476	1.0000
9	GO:0046961	hydrogen ion transporting ATPase activit...	31	21	13.35	16	0.00476	1.00	0.00476	1.0000
10	GO:0016411	acylglycerol O-acyltransferase activity	6	6	2.58	18	0.00635	0.93	0.00635	0.0064
11	GO:0016418	S-acetyltransferase activity	6	6	2.58	19	0.00635	0.83	0.00635	0.0064
12	GO:0019201	nucleotide kinase activity	6	6	2.58	20	0.00635	0.94	0.00635	0.0064
13	GO:0030523	dihydrolipoamide S-acyltransferase activ...	6	6	2.58	21	0.00635	0.83	0.00635	0.0064
14	GO:0016811	hydrolase activity, acting on carbon-nit...	39	25	16.79	22	0.00639	0.90	0.00639	0.0064
15	GO:0003755	peptidyl-prolyl cis-trans isomerase acti...	9	8	3.88	23	0.00653	0.82	0.00653	0.0065
16	GO:0016279	protein-lysine N-methyltransferase activ...	9	8	3.88	24	0.00653	0.61	0.00653	0.4300
17	GO:0016667	oxidoreductase activity, acting on sulfu...	9	8	3.88	25	0.00653	0.99	0.00653	0.0280
18	GO:0003880	C-terminal protein carboxyl methyltransf...	8	7	3.44	28	0.01363	0.76	0.01363	1.0000
19	GO:0009008	DNA-methyltransferase activity	8	7	3.44	29	0.01363	0.71	0.01363	0.0136
20	GO:0004722	protein serine/threonine phosphatase act...	13	10	5.60	31	0.01419	0.68	0.01419	1.0000
21	GO:0003988	acetyl-CoA C-acyltransferase activity	5	5	2.15	32	0.01477	0.48	0.01477	0.0148
22	GO:0004129	cytochrome-c oxidase activity	5	5	2.15	33	0.01477	0.99	0.01477	1.0000
23	GO:0004379	glycylpeptide N-tetradecanoyltransferase...	5	5	2.15	34	0.01477	0.84	0.01477	0.0148
24	GO:0008121	ubiquinol-cytochrome-c reductase activit...	5	5	2.15	35	0.01477	0.99	0.01477	1.0000
25	GO:0015002	heme-copper terminal oxidase activity	5	5	2.15	36	0.01477	0.99	0.01477	1.0000
26	GO:0016419	S-malonyltransferase activity	5	5	2.15	37	0.01477	0.87	0.01477	0.0148
27	GO:0016420	malonyltransferase activity	5	5	2.15	38	0.01477	0.87	0.01477	1.0000
28	GO:0016675	oxidoreductase activity, acting on heme ...	5	5	2.15	39	0.01477	0.99	0.01477	1.0000
29	GO:0016676	oxidoreductase activity, acting on heme ...	5	5	2.15	40	0.01477	0.99	0.01477	1.0000
30	GO:0016681	oxidoreductase activity, acting on diphe...	5	5	2.15	41	0.01477	0.99	0.01477	1.0000
31	GO:0016749	N-succinyltransferase activity	5	5	2.15	42	0.01477	1.00	0.01477	0.0148
32	GO:0019107	myristoyltransferase activity	5	5	2.15	43	0.01477	0.84	0.01477	1.0000
33	GO:0009055	electron carrier activity	30	19	12.92	45	0.01996	0.86	0.01996	0.5697
34	GO:0008565	protein transporter activity	80	44	34.45	46	0.02024	0.96	0.02024	0.0202
35	GO:0000158	protein phosphatase type 2A activity	10	8	4.31	47	0.02027	0.74	0.02027	0.0203
36	GO:0000163	protein phosphatase type 1 activity	10	8	4.31	48	0.02027	0.74	0.02027	1.0000
37	GO:0004723	calcium-dependent protein serine/threoni...	10	8	4.31	49	0.02027	0.74	0.02027	0.0203
38	GO:0004724	magnesium-dependent protein serine/threo...	10	8	4.31	50	0.02027	0.74	0.02027	0.0203
39	GO:0008420	CTD phosphatase activity	10	8	4.31	51	0.02027	0.74	0.02027	0.0203
40	GO:0008597	calcium-dependent protein serine/threoni...	10	8	4.31	52	0.02027	0.74	0.02027	0.0203
41	GO:0015071	protein phosphatase type 2C activity	10	8	4.31	53	0.02027	0.74	0.02027	0.0203
42	GO:0017018	myosin phosphatase activity	10	8	4.31	54	0.02027	0.74	0.02027	0.0203
43	GO:0017020	myosin phosphatase regulator activity	10	8	4.31	55	0.02027	0.74	0.02027	0.0203
44	GO:0030357	protein phosphatase type 2B activity	10	8	4.31	56	0.02027	0.74	0.02027	0.0203
45	GO:0016772	transferase activity, transferring phosp...	393	200	169.23	9	0.00073	1.00	0.02377	0.8848
46	GO:0004040	amidase activity	21	14	9.04	58	0.02494	0.87	0.02494	1.0000
47	GO:0016408	C-acyltransferase activity	12	9	5.17	59	0.02592	0.65	0.02592	1.0000
48	GO:0004840	ubiquitin conjugating enzyme activity	23	15	9.90	61	0.02669	0.92	0.02669	0.0267
49	GO:0008639	small protein conjugating enzyme activit...	23	15	9.90	62	0.02669	0.92	0.02669	0.6748
50	GO:0000179	rRNA (adenine-N6,N6-)-dimethyltransferas...	7	6	3.01	63	0.02808	0.66	0.02808	0.0281
51	GO:0008174	mRNA methyltransferase activity	7	6	3.01	64	0.02808	0.66	0.02808	0.0281
52	GO:0008326	site-specific DNA-methyltransferase (cyt...	7	6	3.01	65	0.02808	0.66	0.02808	1.0000

53	GO:0008649	rRNA methyltransferase activity	7	6	3.01	66	0.02808	0.66	0.02808	1.0000
54	GO:0008650	rRNA (uridine-2’-O-)-methyltransferase a...	7	6	3.01	67	0.02808	0.66	0.02808	0.0281
55	GO:0009383	rRNA (cytosine-C5-967)-methyltransferase...	7	6	3.01	68	0.02808	0.66	0.02808	0.0281
56	GO:0016205	selenocysteine methyltransferase activit...	7	6	3.01	69	0.02808	0.66	0.02808	0.0281
57	GO:0016273	arginine N-methyltransferase activity	7	6	3.01	70	0.02808	0.66	0.02808	1.0000
58	GO:0016274	protein-arginine N-methyltransferase act...	7	6	3.01	71	0.02808	0.66	0.02808	0.0281
59	GO:0016300	tRNA (uracil) methyltransferase activity	7	6	3.01	72	0.02808	0.66	0.02808	0.0281
60	GO:0016424	tRNA (guanosine) methyltransferase activ...	7	6	3.01	73	0.02808	0.66	0.02808	0.0281
61	GO:0016426	tRNA (adenine)-methyltransferase activit...	7	6	3.01	74	0.02808	0.66	0.02808	0.0281
62	GO:0016427	tRNA (cytosine)-methyltransferase activi...	7	6	3.01	75	0.02808	0.66	0.02808	0.0281
63	GO:0016431	tRNA (uridine) methyltransferase activit...	7	6	3.01	76	0.02808	0.66	0.02808	0.0281
64	GO:0016433	rRNA (adenine) methyltransferase activit...	7	6	3.01	77	0.02808	0.66	0.02808	1.0000
65	GO:0016434	rRNA (cytosine) methyltransferase activi...	7	6	3.01	78	0.02808	0.66	0.02808	1.0000
66	GO:0016435	rRNA (guanine) methyltransferase activit...	7	6	3.01	79	0.02808	0.66	0.02808	0.0281
67	GO:0016436	rRNA (uridine) methyltransferase activit...	7	6	3.01	80	0.02808	0.66	0.02808	1.0000
68	GO:0016774	phosphotransferase activity, carboxyl gr...	7	6	3.01	81	0.02808	0.99	0.02808	0.0281
69	GO:0018423	protein-leucine O-methyltransferase acti...	7	6	3.01	82	0.02808	0.66	0.02808	1.0000
70	GO:0018707	1-phenanthrol methyltransferase activity	7	6	3.01	83	0.02808	0.66	0.02808	0.0281
71	GO:0019702	protein-arginine N5-methyltransferase ac...	7	6	3.01	84	0.02808	0.66	0.02808	0.0281
72	GO:0030792	methylarsonite methyltransferase activit...	7	6	3.01	85	0.02808	0.66	0.02808	0.0281
73	GO:0005198	structural molecule activity	150	122	64.59	1	2.2e-22	1.00	0.02869	2.2e-22
74	GO:0004812	aminoacyl-tRNA ligase activity	51	29	21.96	86	0.03221	0.96	0.03221	0.0322
75	GO:0016875	ligase activity, forming carbon-oxygen b...	51	29	21.96	87	0.03221	0.96	0.03221	1.0000
76	GO:0016876	ligase activity, forming aminoacyl-tRNA ...	51	29	21.96	88	0.03221	0.96	0.03221	0.3695
77	GO:0003747	translation release factor activity	4	4	1.72	90	0.03433	0.73	0.03433	0.0343
78	GO:0003958	NADPH-hemoprotein reductase activity	4	4	1.72	91	0.03433	0.56	0.03433	0.0343
79	GO:0004147	dihydrolipoamide branched chain acyltran...	4	4	1.72	92	0.03433	0.87	0.03433	1.0000
80	GO:0004405	H2A/H2B histone acetyltransferase activi...	4	4	1.72	93	0.03433	0.87	0.03433	0.0343
81	GO:0004406	H3/H4 histone acetyltransferase activity	4	4	1.72	94	0.03433	0.87	0.03433	0.0343
82	GO:0004594	pantothenate kinase activity	4	4	1.72	95	0.03433	0.80	0.03433	0.0343
83	GO:0004839	ubiquitin activating enzyme activity	4	4	1.72	96	0.03433	0.99	0.03433	0.0343
84	GO:0005199	structural constituent of cell wall	4	4	1.72	97	0.03433	0.93	0.03433	1.0000
85	GO:0008079	translation termination factor activity	4	4	1.72	98	0.03433	0.73	0.03433	1.0000
86	GO:0008252	nucleotidase activity	4	4	1.72	99	0.03433	0.99	0.03433	0.0343
87	GO:0008320	protein carrier activity	4	4	1.72	100	0.03433	0.97	0.03433	1.0000
88	GO:0008641	small protein activating enzyme activity	4	4	1.72	101	0.03433	0.99	0.03433	1.0000
89	GO:0008951	palmitoleoyl [acyl-carrier-protein]-depe...	4	4	1.72	102	0.03433	0.87	0.03433	0.0343
90	GO:0015359	amino acid permease activity	4	4	1.72	103	0.03433	1.00	0.03433	0.0343
91	GO:0016406	carnitine O-acyltransferase activity	4	4	1.72	104	0.03433	0.87	0.03433	0.0343
92	GO:0016409	palmitoyltransferase activity	4	4	1.72	105	0.03433	0.87	0.03433	1.0000
93	GO:0016412	serine O-acyltransferase activity	4	4	1.72	106	0.03433	0.87	0.03433	0.0343
94	GO:0016414	O-octanoyltransferase activity	4	4	1.72	107	0.03433	0.87	0.03433	0.0343
95	GO:0016415	octanoyltransferase activity	4	4	1.72	108	0.03433	0.87	0.03433	1.0000
96	GO:0016416	O-palmitoyltransferase activity	4	4	1.72	109	0.03433	0.87	0.03433	0.0343
97	GO:0016454	C-palmitoyltransferase activity	4	4	1.72	110	0.03433	0.87	0.03433	0.0343
98	GO:0016750	O-succinyltransferase activity	4	4	1.72	111	0.03433	0.87	0.03433	0.0343
99	GO:0016752	sinapoyltransferase activity	4	4	1.72	112	0.03433	0.87	0.03433	1.0000
100	GO:0016753	O-sinapoyltransferase activity	4	4	1.72	113	0.03433	0.87	0.03433	0.0343
101	GO:0018030	peptidyl-lysine N6-myristoyltransferase ...	4	4	1.72	114	0.03433	0.87	0.03433	1.0000
102	GO:0018031	peptidyl-lysine N6-palmitoyltransferase ...	4	4	1.72	115	0.03433	0.87	0.03433	0.0343
103	GO:0018711	benzoyl acetate-CoA thiolase activity	4	4	1.72	116	0.03433	0.87	0.03433	0.0343
104	GO:0018712	3-hydroxybutyryl-CoA thiolase activity	4	4	1.72	117	0.03433	0.87	0.03433	0.0343
105	GO:0018713	3-ketopimelyl-CoA thiolase activity	4	4	1.72	118	0.03433	0.87	0.03433	0.0343

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106 GO:0019105             N-palmitoyltransferase activity         4           4     1.72             119 0.03433 0.87 0.03433  1.0000
107 GO:0019186         acyl-CoA N-acyltransferase activity         4           4     1.72             120 0.03433 0.87 0.03433  0.0343
108 GO:0019705 protein-cysteine S-myristoyltransferase ...         4           4     1.72             121 0.03433 0.87 0.03433  0.0343
109 GO:0019706 protein-cysteine S-palmitoleyltransferas...         4           4     1.72             122 0.03433 0.87 0.03433  0.0343
110 GO:0019707 protein-cysteine S-acyltransferase activ...         4           4     1.72             123 0.03433 0.87 0.03433  1.0000
111 GO:0042576            aspartyl aminopeptidase activity         4           4     1.72             124 0.03433 0.86 0.03433  0.0343
112 GO:0046941 azetidine-2-carboxylic acid acetyltransf...         4           4     1.72             125 0.03433 0.87 0.03433  0.0343
113 GO:0004448           isocitrate dehydrogenase activity        16          11     6.89             126 0.03438 0.48 0.03438  0.0344
114 GO:0008172                S-methyltransferase activity        16          11     6.89             127 0.03438 0.97 0.03438  0.0344
115 GO:0016702 oxidoreductase activity, acting on singl...        16          11     6.89             128 0.03438 0.79 0.03438  0.3322
116 GO:0003723                                RNA binding        76          41    32.73             129 0.03548 1.00 0.03548  0.0355
117 GO:0004022              alcohol dehydrogenase activity        18          12     7.75             130 0.03744 0.65 0.03744  0.0374
118 GO:0008137    NADH dehydrogenase (ubiquinone) activity         9           7     3.88             131 0.03849 0.97 0.03849  0.0385
119 GO:0050136       NADH dehydrogenase (quinone) activity         9           7     3.88             132 0.03849 0.97 0.03849  1.0000
120 GO:0005515                            protein binding       125          64    53.83             133 0.03910 0.77 0.03910  0.2388
121 GO:0051213                         dioxygenase activity        20          13     8.61             135 0.03987 0.75 0.03987  0.7127
122 GO:0016779             nucleotidyltransferase activity        77          49    33.16               7 0.00020 0.86 0.04324  0.0004

##########  Cellular component  #############

     GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS    elim  weight
1   GO:0005840                                  ribosome       134         111    62.55               4 6.1e-19 0.997 6.1e-19  1.0000
2   GO:0005737                                 cytoplasm       418         283   195.13               1 9.7e-22 0.999 4.8e-05  0.0031
3   GO:0005743               mitochondrial inner membrane        35          28    16.34              17 5.0e-05 0.946 5.0e-05  1.0000
4   GO:0044446               intracellular organelle part       242         159   112.97               8 2.5e-10 0.957  0.0012  0.0066
5   GO:0044429                        mitochondrial part        58          46    27.07              11 2.7e-07 0.984  0.0017  1.0000
6   GO:0043234                          protein complex       475         299   221.73               7 1.1e-15 0.996  0.0031  0.0044
7   GO:0005732 small nucleolar ribonucleoprotein comple...        16          13     7.47              27 0.00501 0.962  0.0050  1.0000
8   GO:0000786                              nucleosome        13          11     6.07              28 0.00577 0.925  0.0058  0.4649
9   GO:0005839 proteasome core complex (sensu Eukaryota...        13          11     6.07              29 0.00577 0.625  0.0058  0.4649
10  GO:0015935                  small ribosomal subunit        12          10     5.60              31 0.01063 0.993  0.0106  1.0000
11  GO:0016469 proton-transporting two-sector ATPase co...        34          23    15.87              32 0.01064 0.998  0.0106  0.4639
12  GO:0008287 protein serine/threonine phosphatase com...        14          11     6.54              34 0.01557 0.506  0.0156  1.0000
13  GO:0005759                     mitochondrial matrix        11           9     5.13              36 0.01934 0.931  0.0193  0.0606
14  GO:0031980                      mitochondrial lumen        11           9     5.13              37 0.01934 0.931  0.0193  1.0000
15  GO:0031974                 membrane-enclosed lumen        46          33    21.47              21 0.00045 0.894  0.0199  0.7104
16  GO:0043233                         organelle lumen        46          33    21.47              22 0.00045 0.894  0.0199  1.0000
17  GO:0005829                                 cytosol         5           5     2.33              38 0.02206 0.938  0.0221  1.0000
18  GO:0044445                          cytosolic part         5           5     2.33              39 0.02206 0.938  0.0221  0.0221
19  GO:0015934                  large ribosomal subunit         8           7     3.73              41 0.02268 0.852  0.0227  1.0000
20  GO:0031967                       organelle envelope        62          46    28.94              13 7.7e-06 0.984  0.0251  1.0000
21  GO:0005963 magnesium-dependent protein serine/threo...        10           8     4.67              42 0.03465 0.615  0.0347  0.0347
22  GO:0017023                myosin phosphatase complex        10           8     4.67              43 0.03465 0.615  0.0347  1.0000
23  GO:0005740                    mitochondrial envelope        47          37    21.94              12 5.8e-06 0.988  0.0421 5.8e-06
24  GO:0044444                         cytoplasmic part       305         215   142.38               2 1.7e-19 0.992  0.0431  1.0000
25  GO:0044455               mitochondrial membrane part         7           6     3.27              45 0.04322 0.921  0.0432  1.0000
26  GO:0042721 mitochondrial inner membrane protein ins...         4           4     1.87              46 0.04735 0.954  0.0473  1.0000

##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1   GO:0006412                              translation       231         170   100.96               1 3.5e-21 1.00 1.1e-19 4.6e-21
2   GO:0007264 small GTPase mediated signal transductio...        40          30    17.48              14 5.5e-05 0.98 5.5e-05 5.5e-05
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3	GO:0008654	phospholipid biosynthetic process	20	16	8.74	27	0.00102	0.75	0.0010	0.00463
4	GO:0042254	ribosome biogenesis and assembly	11	10	4.81	30	0.00167	0.93	0.0017	0.00167
5	GO:0016043	cell organization and biogenesis	220	138	96.15	7	4.8e-09	0.99	0.0023	0.85235
6	GO:0006092	main pathways of carbohydrate metabolic ...	59	37	25.79	33	0.00240	0.98	0.0024	0.00240
7	GO:0006886	intracellular protein transport	82	53	35.84	18	9.5e-05	1.00	0.0026	1.00000
8	GO:0006520	amino acid metabolic process	221	117	96.59	37	0.00292	0.99	0.0029	0.86126
9	GO:0009057	macromolecule catabolic process	79	47	34.53	40	0.00319	0.99	0.0032	0.81900
10	GO:0006084	acetyl-CoA metabolic process	18	14	7.87	41	0.00348	1.00	0.0035	0.03614
11	GO:0015986	ATP synthesis coupled proton transport	32	22	13.99	43	0.00363	1.00	0.0036	0.00363
12	GO:0045184	establishment of protein localization	111	73	48.51	9	1.8e-06	1.00	0.0046	0.00015
13	GO:0006606	protein import into nucleus	15	12	6.56	55	0.00467	0.99	0.0047	0.00467
14	GO:0006334	nucleosome assembly	12	10	5.24	58	0.00606	0.99	0.0061	1.00000
15	GO:0006414	translational elongation	9	8	3.93	59	0.00728	1.00	0.0073	1.00000
16	GO:0006397	mRNA processing	26	18	11.36	60	0.00753	0.96	0.0075	0.00753
17	GO:0044248	cellular catabolic process	131	71	57.25	63	0.00920	0.98	0.0092	0.92039
18	GO:0006996	organelle organization and biogenesis	96	62	41.96	12	2.5e-05	0.99	0.0104	0.94587
19	GO:0006790	sulfur metabolic process	23	16	10.05	73	0.01090	0.94	0.0109	0.48994
20	GO:0015031	protein transport	107	70	46.76	11	3.9e-06	1.00	0.0111	0.57927
21	GO:0006464	protein modification	368	182	160.83	76	0.01198	0.97	0.0120	0.02235
22	GO:0065003	macromolecule complex assembly	66	42	28.84	24	0.00081	1.00	0.0144	0.77844
23	GO:0051258	protein polymerization	8	7	3.50	83	0.01498	0.87	0.0150	0.01498
24	GO:0006006	glucose metabolic process	31	20	13.55	84	0.01555	0.99	0.0156	0.01555
25	GO:0044265	cellular macromolecule catabolic process	66	38	28.84	85	0.01560	0.96	0.0156	1.00000
26	GO:0006399	tRNA metabolic process	68	39	29.72	86	0.01563	0.92	0.0156	0.22765
27	GO:0007005	mitochondrion organization and biogenesi...	5	5	2.19	87	0.01590	0.96	0.0159	0.43656
28	GO:0009117	nucleotide metabolic process	85	53	37.15	20	0.00037	0.97	0.0196	0.81527
29	GO:0000051	urea cycle intermediate metabolic proces...	15	11	6.56	90	0.01980	1.00	0.0198	1.00000
30	GO:0006099	tricarboxylic acid cycle	15	11	6.56	91	0.01980	0.99	0.0198	1.00000
31	GO:0006525	arginine metabolic process	15	11	6.56	92	0.01980	1.00	0.0198	0.01980
32	GO:0009060	aerobic respiration	15	11	6.56	93	0.01980	0.99	0.0198	0.43620
33	GO:0009109	coenzyme catabolic process	15	11	6.56	94	0.01980	0.99	0.0198	1.00000
34	GO:0045333	cellular respiration	15	11	6.56	95	0.01980	0.99	0.0198	1.00000
35	GO:0046356	acetyl-CoA catabolic process	15	11	6.56	96	0.01980	0.99	0.0198	1.00000
36	GO:0051187	cofactor catabolic process	15	11	6.56	97	0.01980	0.99	0.0198	1.00000
37	GO:0019538	protein metabolic process	945	496	413.00	4	7.6e-10	1.00	0.0209	0.99260
38	GO:0009059	macromolecule biosynthetic process	288	202	125.87	2	7.7e-21	1.00	0.0223	0.74798
39	GO:0000059	protein import into nucleus, docking	10	8	4.37	100	0.02240	0.99	0.0224	1.00000
40	GO:0006007	glucose catabolic process	28	18	12.24	101	0.02248	0.95	0.0225	0.40442
41	GO:0019320	hexose catabolic process	28	18	12.24	102	0.02248	0.95	0.0225	0.68175
42	GO:0046365	monosaccharide catabolic process	28	18	12.24	103	0.02248	0.95	0.0225	1.00000
43	GO:0016052	carbohydrate catabolic process	30	19	13.11	106	0.02366	0.95	0.0237	1.00000
44	GO:0044275	cellular carbohydrate catabolic process	30	19	13.11	107	0.02366	0.95	0.0237	1.00000
45	GO:0046164	alcohol catabolic process	30	19	13.11	108	0.02366	0.95	0.0237	1.00000
46	GO:0008652	amino acid biosynthetic process	96	52	41.96	110	0.02402	0.96	0.0240	0.19953
47	GO:0007010	cytoskeleton organization and biogenesis	32	20	13.99	111	0.02468	0.90	0.0247	0.10624
48	GO:0030163	protein catabolic process	44	26	19.23	114	0.02822	0.78	0.0282	0.01482
49	GO:0000096	sulfur amino acid metabolic process	12	9	5.24	115	0.02879	1.00	0.0288	0.02239
50	GO:0009309	amine biosynthetic process	99	53	43.27	116	0.02975	0.92	0.0298	0.55789
51	GO:0016044	membrane organization and biogenesis	7	6	3.06	117	0.03041	0.99	0.0304	1.00000
52	GO:0044260	cellular macromolecule metabolic process	938	491	409.95	5	1.6e-09	1.00	0.0304	0.99299
53	GO:0006769	nicotinamide metabolic process	14	10	6.12	119	0.03414	0.97	0.0341	1.00000
54	GO:0009066	aspartate family amino acid metabolic pr...	14	10	6.12	120	0.03414	1.00	0.0341	0.38194
55	GO:0019362	pyridine nucleotide metabolic process	14	10	6.12	121	0.03414	0.97	0.0341	1.00000

56	GO:0006766	vitamin metabolic process	27	17	11.80	122	0.03416	0.95	0.0342	1.00000
57	GO:0006767	water-soluble vitamin metabolic process	27	17	11.80	123	0.03416	0.95	0.0342	1.00000
58	GO:0006807	nitrogen compound metabolic process	262	141	114.50	22	0.00045	0.98	0.0344	0.21898
59	GO:0044267	cellular protein metabolic process	926	485	404.70	6	1.9e-09	1.00	0.0353	0.99029
60	GO:0006354	RNA elongation	4	4	1.75	124	0.03642	0.99	0.0364	0.03642
61	GO:0006415	translational termination	4	4	1.75	125	0.03642	0.70	0.0364	1.00000
62	GO:0006626	protein targeting to mitochondrion	4	4	1.75	126	0.03642	0.97	0.0364	1.00000
63	GO:0007006	mitochondrial membrane organization and ...	4	4	1.75	127	0.03642	0.97	0.0364	1.00000
64	GO:0007007	inner mitochondrial membrane organizatio...	4	4	1.75	128	0.03642	0.97	0.0364	1.00000
65	GO:0008154	actin polymerization and/or depolymeriza...	4	4	1.75	129	0.03642	0.99	0.0364	1.00000
66	GO:0022411	cellular structure disassembly	4	4	1.75	130	0.03642	0.70	0.0364	1.00000
67	GO:0030041	actin filament polymerization	4	4	1.75	131	0.03642	0.99	0.0364	1.00000
68	GO:0043241	protein complex disassembly	4	4	1.75	132	0.03642	0.70	0.0364	1.00000
69	GO:0043624	cellular protein complex disassembly	4	4	1.75	133	0.03642	0.70	0.0364	1.00000
70	GO:0043681	protein import into mitochondrion	4	4	1.75	134	0.03642	0.97	0.0364	1.00000
71	GO:0045039	protein import into mitochondrial inner ...	4	4	1.75	135	0.03642	0.97	0.0364	0.03642
72	GO:0019318	hexose metabolic process	45	26	19.67	137	0.03960	0.99	0.0396	0.94273
73	GO:0006119	oxidative phosphorylation	41	29	17.92	21	0.00041	1.00	0.0410	0.43475
74	GO:0042773	ATP synthesis coupled electron transport	9	7	3.93	138	0.04192	0.96	0.0419	1.00000
75	GO:0042775	ATP synthesis coupled electron transport...	9	7	3.93	139	0.04192	0.96	0.0419	0.04192
76	GO:0009110	vitamin biosynthetic process	18	12	7.87	140	0.04221	0.97	0.0422	0.82076
77	GO:0042364	water-soluble vitamin biosynthetic proce...	18	12	7.87	141	0.04221	0.97	0.0422	0.60625
78	GO:0044271	nitrogen compound biosynthetic process	103	54	45.02	143	0.04462	0.92	0.0446	1.00000
79	GO:0006066	alcohol metabolic process	66	36	28.84	144	0.04865	0.97	0.0486	0.84220
80	GO:0019438	aromatic compound biosynthetic process	24	15	10.49	145	0.04949	0.85	0.0495	0.15447

E.1.4 Imprint category E025

GO term over-representation results for category E025 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############
```

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005524	ATP binding	627	136	94.05	3	1.2e-06	1.000	1.2e-06	0.19767
2	GO:0003677	DNA binding	664	141	99.60	4	2.7e-06	0.531	0.00010	1.00000
3	GO:0004004	ATP-dependent RNA helicase activity	42	15	6.30	19	0.00072	0.899	0.00072	0.00072
4	GO:0015462	protein-transporting ATPase activity	42	15	6.30	20	0.00072	0.899	0.00072	0.00072
5	GO:0015616	DNA translocase activity	42	15	6.30	21	0.00072	0.899	0.00072	0.00072
6	GO:0017116	single-stranded DNA-dependent ATP-depend...	42	15	6.30	22	0.00072	0.899	0.00072	0.00072
7	GO:0042624	ATPase activity, uncoupled	42	15	6.30	23	0.00072	0.899	0.00072	1.00000
8	GO:0016758	transferase activity, transferring hexos...	57	18	8.55	27	0.00117	0.919	0.00117	0.03989
9	GO:0008194	UDP-glycosyltransferase activity	32	12	4.80	28	0.00149	0.907	0.00149	0.00292
10	GO:0008026	ATP-dependent helicase activity	89	30	13.35	9	7.2e-06	0.862	0.00237	1.00000
11	GO:0008047	enzyme activator activity	26	10	3.90	32	0.00295	0.602	0.00295	0.27588
12	GO:0005247	voltage-gated chloride channel activity	3	3	0.45	35	0.00336	1.000	0.00336	0.00336
13	GO:0000156	two-component response regulator activit...	15	7	2.25	37	0.00356	0.977	0.00356	1.00000
14	GO:0003700	transcription factor activity	324	66	48.60	40	0.00441	0.618	0.00441	1.00000
15	GO:0005215	transporter activity	843	161	126.45	17	0.00026	0.994	0.00493	0.03657
16	GO:0004339	glucan 1,4-alpha-glucosidase activity	32	11	4.80	42	0.00509	0.855	0.00509	0.00509
17	GO:0016879	ligase activity, forming carbon-nitrogen...	121	29	18.15	44	0.00577	0.543	0.00577	0.92287

18	GO:0017111	nucleoside-triphosphatase activity	303	75	45.45	5	3.3e-06	0.959	0.00678	0.00025
19	GO:0004683	calmodulin regulated protein kinase acti...	29	10	4.35	46	0.00727	0.438	0.00727	0.00727
20	GO:0016307	phosphatidylinositol phosphate kinase ac...	25	9	3.75	47	0.00784	0.503	0.00784	0.38411
21	GO:0003676	nucleic acid binding	1047	212	157.05	1	2.0e-07	0.522	0.00798	2.7e-07
22	GO:0004221	ubiquitin thiolesterase activity	21	8	3.15	49	0.00820	0.884	0.00820	0.00820
23	GO:0004222	metalloendopeptidase activity	21	8	3.15	50	0.00820	0.491	0.00820	0.00820
24	GO:0019200	carbohydrate kinase activity	34	11	5.10	53	0.00849	0.277	0.00849	0.00849
25	GO:0004713	protein-tyrosine kinase activity	119	28	17.85	54	0.00859	0.985	0.00859	0.07812
26	GO:0001565	phorbol ester receptor activity	22	8	3.30	56	0.01123	0.436	0.01123	1.00000
27	GO:0004675	transmembrane receptor protein serine/th...	22	8	3.30	57	0.01123	0.436	0.01123	0.01123
28	GO:0004676	3-phosphoinositide-dependent protein kin...	22	8	3.30	58	0.01123	0.436	0.01123	0.01123
29	GO:0004677	DNA-dependent protein kinase activity	22	8	3.30	59	0.01123	0.436	0.01123	0.01123
30	GO:0004679	AMP-activated protein kinase activity	22	8	3.30	60	0.01123	0.436	0.01123	0.01123
31	GO:0004681	casein kinase I activity	22	8	3.30	61	0.01123	0.436	0.01123	0.01123
32	GO:0004686	eukaryotic elongation factor-2 kinase ac...	22	8	3.30	62	0.01123	0.436	0.01123	1.00000
33	GO:0004688	multifunctional calcium- and calmodulin-...	22	8	3.30	63	0.01123	0.436	0.01123	1.00000
34	GO:0004689	phosphorylase kinase activity	22	8	3.30	64	0.01123	0.436	0.01123	1.00000
35	GO:0004692	cGMP-dependent protein kinase activity	22	8	3.30	65	0.01123	0.436	0.01123	0.01123
36	GO:0004694	eukaryotic translation initiation factor...	22	8	3.30	66	0.01123	0.436	0.01123	0.01123
37	GO:0004695	galactosyltransferase-associated kinase ...	22	8	3.30	67	0.01123	0.436	0.01123	0.01123
38	GO:0004696	glycogen synthase kinase 3 activity	22	8	3.30	68	0.01123	0.436	0.01123	0.01123
39	GO:0004697	protein kinase C activity	22	8	3.30	69	0.01123	0.436	0.01123	1.00000
40	GO:0004698	calcium-dependent protein kinase C activ...	22	8	3.30	70	0.01123	0.436	0.01123	0.01123
41	GO:0004700	atypical protein kinase C activity	22	8	3.30	71	0.01123	0.436	0.01123	0.01123
42	GO:0004701	diacylglycerol-activated phospholipid-de...	22	8	3.30	72	0.01123	0.436	0.01123	0.01123
43	GO:0004703	G-protein coupled receptor kinase activi...	22	8	3.30	73	0.01123	0.436	0.01123	0.01123
44	GO:0004704	NF-kappaB-inducing kinase activity	22	8	3.30	74	0.01123	0.436	0.01123	0.01123
45	GO:0004705	JUN kinase activity	22	8	3.30	75	0.01123	0.436	0.01123	0.01123
46	GO:0004706	JUN kinase kinase kinase activity	22	8	3.30	76	0.01123	0.436	0.01123	0.01123
47	GO:0004708	MAP kinase kinase activity	22	8	3.30	77	0.01123	0.436	0.01123	1.00000
48	GO:0004709	MAP kinase kinase kinase activity	22	8	3.30	78	0.01123	0.436	0.01123	1.00000
49	GO:0004710	MAP/ERK kinase kinase activity	22	8	3.30	79	0.01123	0.436	0.01123	0.01123
50	GO:0004711	ribosomal protein S6 kinase activity	22	8	3.30	80	0.01123	0.436	0.01123	0.01123
51	GO:0004712	protein threonine/tyrosine kinase activi...	22	8	3.30	81	0.01123	0.436	0.01123	1.00000
52	GO:0004714	transmembrane receptor protein tyrosine ...	22	8	3.30	82	0.01123	0.436	0.01123	0.01123
53	GO:0004715	non-membrane spanning protein tyrosine k...	22	8	3.30	83	0.01123	0.436	0.01123	0.01123
54	GO:0004716	receptor signaling protein tyrosine kina...	22	8	3.30	84	0.01123	0.436	0.01123	1.00000
55	GO:0004718	Janus kinase activity	22	8	3.30	85	0.01123	0.436	0.01123	0.01123
56	GO:0008338	MAP kinase 1 activity	22	8	3.30	86	0.01123	0.436	0.01123	0.01123
57	GO:0008339	MP kinase activity	22	8	3.30	87	0.01123	0.436	0.01123	0.01123
58	GO:0008349	MAP kinase kinase kinase kinase activity	22	8	3.30	88	0.01123	0.436	0.01123	0.01123
59	GO:0008384	IkappaB kinase activity	22	8	3.30	89	0.01123	0.436	0.01123	0.01123
60	GO:0008545	JUN kinase kinase activity	22	8	3.30	90	0.01123	0.436	0.01123	0.01123
61	GO:0008607	phosphorylase kinase regulator activity	22	8	3.30	91	0.01123	0.436	0.01123	0.01123
62	GO:0008819	cobinamide kinase activity	22	8	3.30	92	0.01123	0.436	0.01123	0.01123
63	GO:0016538	cyclin-dependent protein kinase regulato...	22	8	3.30	93	0.01123	0.436	0.01123	0.01123
64	GO:0016908	MAP kinase 2 activity	22	8	3.30	94	0.01123	0.436	0.01123	0.01123
65	GO:0016909	SAP kinase activity	22	8	3.30	95	0.01123	0.436	0.01123	1.00000
66	GO:0018720	phenol kinase activity	22	8	3.30	96	0.01123	0.436	0.01123	0.01123
67	GO:0019199	transmembrane receptor protein kinase ac...	22	8	3.30	97	0.01123	0.436	0.01123	1.00000
68	GO:0019209	kinase activator activity	22	8	3.30	98	0.01123	0.436	0.01123	1.00000
69	GO:0019912	cyclin-dependent protein kinase activati...	22	8	3.30	99	0.01123	0.436	0.01123	0.01123
70	GO:0019914	cyclin-dependent protein kinase activati...	22	8	3.30	100	0.01123	0.436	0.01123	0.01123

71	GO:0030295	protein kinase activator activity	22	8	3.30	101	0.01123	0.436	0.01123	1.00000
72	GO:0042556	eukaryotic elongation factor-2 kinase re...	22	8	3.30	102	0.01123	0.436	0.01123	1.00000
73	GO:0042557	eukaryotic elongation factor-2 kinase ac...	22	8	3.30	103	0.01123	0.436	0.01123	0.01123
74	GO:0004043	L-aminoadipate-semialdehyde dehydrogenas...	14	6	2.10	104	0.01143	0.946	0.01143	0.01143
75	GO:0003984	acetolactate synthase activity	4	3	0.60	106	0.01195	0.999	0.01195	0.01195
76	GO:0004176	ATP-dependent peptidase activity	4	3	0.60	107	0.01195	0.997	0.01195	0.01195
77	GO:0016634	oxidoreductase activity, acting on the C...	4	3	0.60	108	0.01195	0.995	0.01195	0.01195
78	GO:0042625	ATPase activity, coupled to transmembran...	97	23	14.55	112	0.01488	0.958	0.01488	0.07512
79	GO:0004693	cyclin-dependent protein kinase activity	23	8	3.45	113	0.01501	0.541	0.01501	0.01501
80	GO:0008443	phosphofructokinase activity	23	8	3.45	114	0.01501	0.312	0.01501	1.00000
81	GO:0000155	two-component sensor activity	15	6	2.25	116	0.01667	0.990	0.01667	0.01667
82	GO:0004673	protein histidine kinase activity	15	6	2.25	117	0.01667	0.990	0.01667	1.00000
83	GO:0016775	phosphotransferase activity, nitrogenous...	15	6	2.25	118	0.01667	0.990	0.01667	1.00000
84	GO:0004842	ubiquitin-protein ligase activity	77	19	11.55	119	0.01695	0.977	0.01695	0.01695
85	GO:0019787	small conjugating protein ligase activit...	77	19	11.55	120	0.01695	0.977	0.01695	0.67605
86	GO:0016887	ATPase activity	225	59	33.75	8	5.7e-06	0.914	0.02217	0.27083
87	GO:0004066	asparagine synthase (glutamine-hydrolyzi...	2	2	0.30	124	0.02248	0.993	0.02248	0.02248
88	GO:0003684	damaged DNA binding	16	6	2.40	125	0.02337	0.989	0.02337	1.00000
89	GO:0008081	phosphoric diester hydrolase activity	16	6	2.40	126	0.02337	0.992	0.02337	0.62136
90	GO:0035004	phosphoinositide 3-kinase activity	25	8	3.75	131	0.02519	0.142	0.02519	1.00000
91	GO:0004680	casein kinase activity	55	14	8.25	134	0.02903	0.659	0.02903	1.00000
92	GO:0004690	cyclic nucleotide-dependent protein kina...	55	14	8.25	135	0.02903	0.659	0.02903	1.00000
93	GO:0005275	amine transporter activity	87	20	13.05	136	0.03037	0.998	0.03037	1.00000
94	GO:0005279	amino acid-polyamine transporter activit...	87	20	13.05	137	0.03037	0.998	0.03037	0.03037
95	GO:0015171	amino acid transporter activity	87	20	13.05	138	0.03037	0.998	0.03037	0.39664
96	GO:0015203	polyamine transporter activity	87	20	13.05	139	0.03037	0.998	0.03037	0.39664
97	GO:0035251	UDP-glucosyltransferase activity	17	6	2.55	141	0.03165	0.994	0.03165	1.00000
98	GO:0046527	glucosyltransferase activity	17	6	2.55	142	0.03165	0.994	0.03165	1.00000
99	GO:0008812	choline dehydrogenase activity	9	4	1.35	143	0.03381	0.707	0.03381	0.03381
100	GO:0016722	oxidoreductase activity, oxidizing metal...	9	4	1.35	144	0.03381	0.813	0.03381	1.00000
101	GO:0016723	oxidoreductase activity, oxidizing metal...	9	4	1.35	145	0.03381	0.813	0.03381	0.03381
102	GO:0016744	transferase activity, transferring aldeh...	9	4	1.35	146	0.03381	0.980	0.03381	1.00000
103	GO:0005342	organic acid transporter activity	89	20	13.35	147	0.03790	0.998	0.03790	1.00000
104	GO:0046943	carboxylic acid transporter activity	89	20	13.35	148	0.03790	0.998	0.03790	1.00000
105	GO:0004702	receptor signaling protein serine/threon...	27	8	4.05	149	0.03938	0.466	0.03938	1.00000
106	GO:0004707	MAP kinase activity	27	8	4.05	150	0.03938	0.466	0.03938	1.00000
107	GO:0005057	receptor signaling protein activity	27	8	4.05	151	0.03938	0.466	0.03938	1.00000
108	GO:0004888	transmembrane receptor activity	52	13	7.80	153	0.03970	0.080	0.03970	0.85588
109	GO:0016881	acid-amino acid ligase activity	90	20	13.50	154	0.04213	0.860	0.04213	0.85539
110	GO:0019207	kinase regulator activity	58	14	8.70	155	0.04412	0.825	0.04412	1.00000
111	GO:0019887	protein kinase regulator activity	58	14	8.70	156	0.04412	0.825	0.04412	0.76615
112	GO:0004620	phospholipase activity	23	7	3.45	157	0.04596	0.650	0.04596	0.04596
113	GO:0030695	GTPase regulator activity	14	5	2.10	158	0.04653	0.929	0.04653	0.47700
114	GO:0003825	alpha,alpha-trehalose-phosphate synthase...	6	3	0.90	159	0.04725	0.998	0.04725	1.00000
115	GO:0004396	hexokinase activity	6	3	0.90	160	0.04725	0.983	0.04725	1.00000
116	GO:0004499	dimethylaniline monooxygenase (N-oxide-f...	6	3	0.90	161	0.04725	0.944	0.04725	0.04725
117	GO:0004629	phospholipase C activity	6	3	0.90	162	0.04725	0.979	0.04725	1.00000
118	GO:0016884	carbon-nitrogen ligase activity, with gl...	10	4	1.50	163	0.04981	0.119	0.04981	1.00000

########## Cellular component #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight

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1  GO:0005798                   Golgi-associated vesicle         7           4     1.13               1   0.016 0.77 0.016  1.000
2  GO:0016459                             myosin complex         5           3     0.81               2   0.033 1.00 0.033  0.033
3  GO:0000151                   ubiquitin ligase complex        57          15     9.24               3   0.033 0.77 0.033  0.033
4  GO:0012505                        endomembrane system        44          12     7.13               4   0.042 0.90 0.042  1.000

##########  Biological process  #############


       GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1  GO:0009987                           cellular process      3849         637   590.05               1 6.1e-08 0.96 1.7e-06 0.00320
2  GO:0006355 regulation of transcription, DNA-depende...       395          86    60.55               6 0.00023 0.84 0.00023 0.00026
3  GO:0006298                            mismatch repair        11           6     1.69              20 0.00294 0.66 0.00294 0.00294
4  GO:0006821                          chloride transport         3           3     0.46              22 0.00359 1.00 0.00359 0.00359
5  GO:0006261              DNA-dependent DNA replication        23          12     3.53               3 4.1e-05 0.95 0.00497 0.00497
6  GO:0000160 two-component signal transduction system...        21           8     3.22              23 0.00933 0.99 0.00933 0.00933
7  GO:0006270                DNA replication initiation         7           4     1.07              25 0.01302 1.00 0.01302 1.00000
8  GO:0030258                        lipid modification         7           4     1.07              26 0.01302 0.43 0.01302 0.01302
9  GO:0016567                    protein ubiquitination        55          15     8.43              27 0.01569 0.98 0.01569 0.01569
10 GO:0032446 protein modification by small protein co...       55          15     8.43              28 0.01569 0.98 0.01569 0.56145
11 GO:0022402                          cell cycle process        23           8     3.53              31 0.01698 0.83 0.01698 1.00000
12 GO:0006529            asparagine biosynthetic process         2           2     0.31              34 0.02347 0.99 0.02347 0.02347
13 GO:0042981                    regulation of apoptosis         2           2     0.31              35 0.02347 0.95 0.02347 1.00000
14 GO:0043067         regulation of programmed cell death        2           2     0.31              36 0.02347 0.95 0.02347 1.00000
15 GO:0044238                  primary metabolic process      2361         403   361.94              13 0.00046 0.84 0.02564 0.97851
16 GO:0006188                  IMP biosynthetic process         5           3     0.77              39 0.02817 0.92 0.02817 1.00000
17 GO:0006189          'de novo' IMP biosynthetic process       5           3     0.77              40 0.02817 0.92 0.02817 0.02817
18 GO:0046040                     IMP metabolic process         5           3     0.77              41 0.02817 0.92 0.02817 1.00000
19 GO:0006810                               transport       940         165   144.10              33 0.02033 0.99 0.03204 0.28802
20 GO:0006112           energy reserve metabolic process         9           4     1.38              43 0.03633 1.00 0.03633 1.00000
21 GO:0050794              regulation of cellular process      437          97    66.99               2 4.0e-05 0.86 0.03649 1.00000
22 GO:0051234               establishment of localization      944         165   144.71              37 0.02366 0.99 0.03687 1.00000
23 GO:0006865                        amino acid transport        87          20    13.34              44 0.03701 1.00 0.03701 0.03701
24 GO:0015837                             amine transport        87          20    13.34              45 0.03701 1.00 0.03701 1.00000
25 GO:0015849                      organic acid transport        87          20    13.34              46 0.03701 1.00 0.03701 1.00000
26 GO:0046942                   carboxylic acid transport        87          20    13.34              47 0.03701 1.00 0.03701 0.46297
27 GO:0051179                               localization       945         165   144.87              38 0.02456 0.99 0.03816 0.10760
28 GO:0000074 regulation of progression through cell c...       18           6     2.76              48 0.04566 0.70 0.04566 0.04566
29 GO:0051726                    regulation of cell cycle        18           6     2.76              49 0.04566 0.70 0.04566 1.00000
30 GO:0005975             carbohydrate metabolic process       302          57    46.30              50 0.04862 0.99 0.04862 0.13165
```

E.1.5 Imprint category E050

GO term over-representation results for category E050 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0004096                    catalase activity        10           5     1.13               2  0.0028  0.9999 0.0028 0.0028
2   GO:0016646 oxidoreductase activity, acting on the C...        11           5     1.25               3  0.0047  0.5455 0.0047 0.0047
3   GO:0005506                     iron ion binding        65          15     7.37               4  0.0051  0.3940 0.0051 0.0051
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4	GO:0016783	sulfurtransferase activity	4	3	0.45	5	0.0053	0.9947	0.0053	0.0053
5	GO:0016491	oxidoreductase activity	1146	159	129.89	1	0.0017	0.1041	0.0095	0.4707
6	GO:0004737	pyruvate decarboxylase activity	2	2	0.23	8	0.0128	0.9980	0.0128	0.0128
7	GO:0004792	thiosulfate sulfurtransferase activity	2	2	0.23	9	0.0128	0.9973	0.0128	1.0000
8	GO:0004497	monooxygenase activity	241	38	27.32	10	0.0205	0.0428	0.0205	0.0716
9	GO:0004534	5’-3’ exoribonuclease activity	6	3	0.68	11	0.0223	0.7803	0.0223	0.0223
10	GO:0008409	5’-3’ exonuclease activity	6	3	0.68	12	0.0223	0.7803	0.0223	1.0000
11	GO:0050112	inositol 2-dehydrogenase activity	6	3	0.68	13	0.0223	0.3749	0.0223	0.0223
12	GO:0004252	serine-type endopeptidase activity	39	9	4.42	16	0.0273	0.6666	0.0273	0.0273
13	GO:0004033	aldo-keto reductase activity	16	5	1.81	17	0.0277	0.0396	0.0277	0.3576
14	GO:0005351	sugar porter activity	99	18	11.22	18	0.0278	0.9822	0.0278	0.0278
15	GO:0051119	sugar transporter activity	99	18	11.22	19	0.0278	0.9822	0.0278	0.6574
16	GO:0015144	carbohydrate transporter activity	101	18	11.45	21	0.0333	0.9819	0.0333	0.6142
17	GO:0000250	lanosterol synthase activity	3	2	0.34	22	0.0356	0.6180	0.0356	0.0356
18	GO:0003838	sterol 24-C-methyltransferase activity	3	2	0.34	23	0.0356	0.7632	0.0356	0.0356
19	GO:0004735	pyrroline-5-carboxylate reductase activi...	3	2	0.34	24	0.0356	0.5464	0.0356	1.0000
20	GO:0004834	tryptophan synthase activity	3	2	0.34	25	0.0356	0.9827	0.0356	0.0356
21	GO:0005529	sugar binding	3	2	0.34	26	0.0356	0.9795	0.0356	0.0356
22	GO:0008574	plus-end-directed microtubule motor acti...	3	2	0.34	27	0.0356	0.9478	0.0356	0.0356
23	GO:0008678	2-deoxy-D-gluconate 3-dehydrogenase acti...	3	2	0.34	28	0.0356	0.9595	0.0356	0.0356
24	GO:0008810	cellulase activity	3	2	0.34	29	0.0356	0.9998	0.0356	0.0356
25	GO:0031559	oxidosqualene cyclase activity	3	2	0.34	30	0.0356	0.6180	0.0356	1.0000
26	GO:0004194	pepsin A activity	12	4	1.36	32	0.0385	0.9836	0.0385	0.0385
27	GO:0008169	C-methyltransferase activity	12	4	1.36	33	0.0385	0.3953	0.0385	1.0000

########## Cellular component ##############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005851	eukaryotic translation initiation factor...	5	2	0.50	1	0.082	0.52993	0.082	0.082

########## Biological process ##############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0046483	heterocycle metabolic process	52	13	5.70	1	0.0032	0.8567	0.0032	1.0000
2	GO:0006118	electron transport	599	86	65.61	2	0.0034	0.0045	0.0034	0.0035
3	GO:0006783	heme biosynthetic process	5	3	0.55	3	0.0110	0.9850	0.0110	0.0110
4	GO:0042168	heme metabolic process	5	3	0.55	4	0.0110	0.9850	0.0110	1.0000
5	GO:0006800	oxygen and reactive oxygen species metab...	30	8	3.29	5	0.0129	0.9424	0.0129	0.0129
6	GO:0006720	isoprenoid metabolic process	19	6	2.08	6	0.0131	0.8726	0.0131	1.0000
7	GO:0008299	isoprenoid biosynthetic process	19	6	2.08	7	0.0131	0.8726	0.0131	0.0131
8	GO:0008643	carbohydrate transport	101	18	11.06	8	0.0244	0.9848	0.0244	0.0244
9	GO:0009410	response to xenobiotic stimulus	22	6	2.41	9	0.0271	0.7653	0.0271	0.3695
10	GO:0051341	regulation of oxidoreductase activity	34	8	3.72	10	0.0272	0.3271	0.0272	0.0272
11	GO:0006302	double-strand break repair	3	2	0.33	11	0.0333	0.9908	0.0333	0.0333
12	GO:0032501	multicellular organismal process	3	2	0.33	12	0.0333	0.6493	0.0333	0.2067
13	GO:0006979	response to oxidative stress	23	6	2.52	13	0.0334	0.9241	0.0334	1.0000
14	GO:0006206	pyrimidine base metabolic process	12	4	1.31	14	0.0344	0.8702	0.0344	0.0344
15	GO:0042221	response to chemical stimulus	99	17	10.84	16	0.0388	0.7328	0.0388	0.0251
16	GO:0009084	glutamine family amino acid biosynthetic...	24	6	2.63	17	0.0405	0.8908	0.0405	0.0405
17	GO:0006561	proline biosynthetic process	8	3	0.88	18	0.0480	0.8183	0.0480	1.0000
18	GO:0006568	tryptophan metabolic process	8	3	0.88	19	0.0480	0.8224	0.0480	0.0480
19	GO:0006586	indolalkylamine metabolic process	8	3	0.88	20	0.0480	0.8224	0.0480	1.0000
20	GO:0042430	indole and derivative metabolic process	8	3	0.88	21	0.0480	0.8224	0.0480	1.0000

```
21  GO:0042434        indole derivative metabolic process        8          3     0.88             22  0.0480 0.8224 0.0480 1.0000
```

E.1.6 Imprint category E075

GO term over-representation results for category E075 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0016787                         hydrolase activity      1230          83    66.10               1   0.011  0.1955 0.011  0.954
2   GO:0004553 hydrolase activity, hydrolyzing O-glycos...       223          20    11.98               2   0.016  0.4650 0.016  0.595
3   GO:0003824                         catalytic activity      3853         224   207.05               3   0.017 5.1e-06 0.017  0.947
4   GO:0016798 hydrolase activity, acting on glycosyl b...       225          20    12.09               4   0.018  0.4572 0.018  0.715
5   GO:0008318          protein prenyltransferase activity        14           3     0.75               5   0.036  0.9342 0.036  0.097
6   GO:0003973        (S)-2-hydroxy-acid oxidase activity         6           2     0.32               6   0.037  0.9803 0.037  1.000
7   GO:0004867 serine-type endopeptidase inhibitor acti...         6           2     0.32               7   0.037  0.9489 0.037  0.037
8   GO:0008891                 glycolate oxidase activity         6           2     0.32               8   0.037  0.9803 0.037  0.037
9   GO:0004556                     alpha-amylase activity        15           3     0.81               9   0.043  0.8229 0.043  0.043
10  GO:0016160                           amylase activity        15           3     0.81              10   0.043  0.8229 0.043  1.000
11  GO:0016846               carbon-sulfur lyase activity        26           4     1.40              11   0.048  0.6805 0.048  0.048

##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0016021                     integral to membrane       698          48    34.90               1  0.0053 0.04011 0.0053 0.0053
2   GO:0009339                 glycolate oxidase complex         6           2     0.30               5  0.0326 0.96477 0.0326 0.0326
3   GO:0005941               unlocalized protein complex        28           4     1.40               6  0.0480 0.27553 0.0480 0.4807

##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS  elim weight
1   GO:0009141 nucleoside triphosphate metabolic proces...        38           6     2.03               1   0.014 0.90 0.014  1.000
2   GO:0009063               amino acid catabolic process        22           4     1.18               2   0.027 0.99 0.027  1.000
3   GO:0009310                   amine catabolic process        23           4     1.23               3   0.032 0.99 0.032  1.000
4   GO:0044270        nitrogen compound catabolic process        23           4     1.23               4   0.032 0.99 0.032  1.000
5   GO:0009144 purine nucleoside triphosphate metabolic...        34           5     1.82               5   0.033 0.92 0.033  1.000
6   GO:0009145 purine nucleoside triphosphate biosynthe...        34           5     1.82               6   0.033 0.92 0.033  1.000
7   GO:0009199 ribonucleoside triphosphate metabolic pr...        34           5     1.82               7   0.033 0.92 0.033  1.000
8   GO:0009201 ribonucleoside triphosphate biosynthetic...        34           5     1.82               8   0.033 0.92 0.033  1.000
9   GO:0009205 purine ribonucleoside triphosphate metab...        34           5     1.82               9   0.033 0.92 0.033  1.000
10  GO:0009206 purine ribonucleoside triphosphate biosy...        34           5     1.82              10   0.033 0.92 0.033  1.000
11  GO:0009147 pyrimidine nucleoside triphosphate metab...         6           2     0.32              11   0.037 0.58 0.037  1.000
12  GO:0042221              response to chemical stimulus        99          10     5.29              12   0.038 0.77 0.038  0.065
13  GO:0009142 nucleoside triphosphate biosynthetic pro...        36           5     1.92              13   0.041 0.91 0.041  1.000
14  GO:0009150     purine ribonucleotide metabolic process        49           6     2.62              14   0.045 0.30 0.045  1.000
15  GO:0009152 purine ribonucleotide biosynthetic proce...        49           6     2.62              15   0.045 0.30 0.045  1.000
```

E.1.7 Imprint category E1

GO term over-representation results for category E1 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

         GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0018731 1-oxa-2-oxocycloheptane lactonase activi...         6           2     0.20               1   0.015 0.18867 0.015  0.015
2   GO:0018732             sulfolactone hydrolase activity         6           2     0.20               2   0.015 0.18867 0.015  0.015
3   GO:0018733      3,4-dihydrocoumarin hydrolase activity         6           2     0.20               3   0.015 0.18867 0.015  0.015
4   GO:0018734            butyrolactone hydrolase activity         6           2     0.20               4   0.015 0.18867 0.015  0.015
5   GO:0004339       glucan 1,4-alpha-glucosidase activity        32           4     1.06               5   0.020 0.58077 0.020  0.020
6   GO:0004029       aldehyde dehydrogenase (NAD) activity         7           2     0.23               6   0.021 0.71113 0.021  0.021
7   GO:0015926                        glucosidase activity        51           5     1.69               7   0.026 0.26446 0.026  0.392
8   GO:0016620 oxidoreductase activity, acting on the a...        35           4     1.16               8   0.027 0.78701 0.027  1.000
9   GO:0000774 adenyl-nucleotide exchange factor activi...         1           1     0.03               9   0.033 0.99999 0.033  0.033
10  GO:0000907              sulfonate dioxygenase activity         1           1     0.03              10   0.033 0.99928 0.033  0.033
11  GO:0004607 phosphatidylcholine-sterol O-acyltransfe...         1           1     0.03              11   0.033 0.99846 0.033  0.033
12  GO:0004750     ribulose-phosphate 3-epimerase activity         1           1     0.03              12   0.033 0.99910 0.033  0.033
13  GO:0004835            tubulin-tyrosine ligase activity         1           1     0.03              13   0.033 0.99844 0.033  0.033
14  GO:0008793 aromatic-amino-acid transaminase activit...         1           1     0.03              14   0.033 0.99903 0.033  0.033
15  GO:0018479 benzaldehyde dehydrogenase (NAD+) activi...         1           1     0.03              15   0.033 0.99858 0.033  0.033
16  GO:0018602 2,4-dichlorophenoxyacetate alpha-ketoglu...         1           1     0.03              16   0.033 0.99928 0.033  0.033
17  GO:0019115         benzaldehyde dehydrogenase activity         1           1     0.03              17   0.033 0.99858 0.033  1.000
18  GO:0019798    procollagen-proline dioxygenase activity         1           1     0.03              18   0.033 0.99928 0.033  0.033
19  GO:0031543       peptidyl-proline dioxygenase activity         1           1     0.03              19   0.033 0.99928 0.033  1.000
20  GO:0042803           protein homodimerization activity         1           1     0.03              20   0.033 0.99999 0.033  0.033
21  GO:0045432     leucoanthocyanidin dioxygenase activity         1           1     0.03              21   0.033 0.99928 0.033  0.033
22  GO:0045442 deacetoxycephalosporin C hydroxylase act...         1           1     0.03              22   0.033 0.99928 0.033  0.033
23  GO:0046027 phospholipid:diacylglycerol acyltransfer...         1           1     0.03              23   0.033 0.99846 0.033  0.033
24  GO:0046559               alpha-glucuronidase activity         1           1     0.03              24   0.033 0.99949 0.033  0.033
25  GO:0004659                 prenyltransferase activity        22           3     0.73              25   0.035 0.17810 0.035  0.035
26  GO:0016903 oxidoreductase activity, acting on the a...        41           4     1.36              26   0.045 0.89841 0.045  1.000
27  GO:0004930         G-protein coupled receptor activity        25           3     0.83              27   0.048 0.03651 0.048  1.000

##########  Cellular component  #############

         GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0005950              anthranilate synthase complex         1           1     0.03               1   0.031 0.99999 0.031  0.031

##########  Biological process  #############

         GO.ID                                    Term Annotated Significant Expected Rank in classic classic     KS  elim weight
1   GO:0006281                              DNA repair        74           6     2.33               1   0.028 0.7183 0.028  0.028
2   GO:0006974            response to DNA damage stimulus        74           6     2.33               2   0.028 0.7183 0.028  1.000
3   GO:0009719            response to endogenous stimulus        74           6     2.33               3   0.028 0.7183 0.028  1.000
4   GO:0044247 cellular polysaccharide catabolic proces...         1           1     0.03               4   0.031 0.9995 0.031  1.000
5   GO:0045491                    xylan metabolic process         1           1     0.03               5   0.031 0.9995 0.031  1.000
6   GO:0045493                    xylan catabolic process         1           1     0.03               6   0.031 0.9995 0.031  0.031
7   GO:0000041             transition metal ion transport        11           2     0.35               7   0.045 0.9472 0.045  0.045
8   GO:0006298                         mismatch repair        11           2     0.35               8   0.045 0.7954 0.045  1.000
9   GO:0018342                      protein prenylation        11           2     0.35               9   0.045 0.8423 0.045  1.000
```

```
10  GO:0018346              protein amino acid prenylation        11           2     0.35              10   0.045 0.8423 0.045  0.045
11  GO:0045005 maintenance of fidelity during DNA-depen...        11           2     0.35              11   0.045 0.7954 0.045  1.000
```

E.1.8 Imprint category E2

GO term over-representation results for category E2 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS    elim  weight
1   GO:0004058 aromatic-L-amino-acid decarboxylase acti...         3           3     0.18               2 0.00021 0.99197 0.00021 0.00021
2   GO:0004067                       asparaginase activity         6           3     0.36               5 0.00364 0.78917 0.00364 0.00364
3   GO:0016614 oxidoreductase activity, acting on CH-OH...       240          24    14.26               7 0.00790 0.00301 0.00790 0.72861
4   GO:0018585                 fluorene oxygenase activity        22           5     1.31               9 0.00818 0.37212 0.00818 0.00818
5   GO:0018586          mono-butyltin dioxygenase activity        22           5     1.31              10 0.00818 0.37212 0.00818 0.00818
6   GO:0018587           limonene 8-monooxygenase activity        22           5     1.31              11 0.00818 0.37212 0.00818 0.00818
7   GO:0018588         tri-n-butyltin dioxygenase activity        22           5     1.31              12 0.00818 0.37212 0.00818 0.00818
8   GO:0018589          di-n-butyltin dioxygenase activity        22           5     1.31              13 0.00818 0.37212 0.00818 0.00818
9   GO:0018590      methylsilanetriol hydroxylase activity        22           5     1.31              14 0.00818 0.37212 0.00818 0.00818
10  GO:0018591 methyl tertiary butyl ether 3-monooxygen...        22           5     1.31              15 0.00818 0.37212 0.00818 0.00818
11  GO:0018592    4-nitrocatechol 4-monooxygenase activity        22           5     1.31              16 0.00818 0.37212 0.00818 0.00818
12  GO:0018593 4-chlorophenoxyacetate monooxygenase act...        22           5     1.31              17 0.00818 0.37212 0.00818 0.00818
13  GO:0018594 tert-butyl alcohol 2-monooxygenase activ...        22           5     1.31              18 0.00818 0.37212 0.00818 0.00818
14  GO:0018595         alpha-pinene monooxygenase activity        22           5     1.31              19 0.00818 0.37212 0.00818 0.00818
15  GO:0018596     dimethylsilanediol hydroxylase activity        22           5     1.31              20 0.00818 0.37212 0.00818 0.00818
16  GO:0018597              ammonia monooxygenase activity        22           5     1.31              21 0.00818 0.37212 0.00818 0.00818
17  GO:0018598 hydroxymethylsilanetriol oxidase activit...        22           5     1.31              22 0.00818 0.37212 0.00818 0.00818
18  GO:0018599 2-hydroxyisobutyrate 3-monooxygenase act...        22           5     1.31              23 0.00818 0.37212 0.00818 0.00818
19  GO:0018600         alpha-pinene dehydrogenase activity        22           5     1.31              24 0.00818 0.37212 0.00818 0.00818
20  GO:0018601      4-nitrophenol 2-monooxygenase activity        22           5     1.31              25 0.00818 0.37212 0.00818 0.00818
21  GO:0004497                       monooxygenase activity       241          27    14.32               3 0.00096 0.04957 0.00903 0.10255
22  GO:0004448           isocitrate dehydrogenase activity        16           4     0.95              26 0.01261 0.68879 0.01261 0.01261
23  GO:0016616 oxidoreductase activity, acting on the C...       188          19    11.17              27 0.01548 0.00716 0.01548 0.86588
24  GO:0003960            NADPH:quinone reductase activity        17           4     1.01              28 0.01573 0.00093 0.01573 0.01573
25  GO:0008493           tetracycline transporter activity        36           6     2.14              30 0.01804 0.99231 0.01804 1.00000
26  GO:0015307           drug:hydrogen antiporter activity        36           6     2.14              31 0.01804 0.99231 0.01804 1.00000
27  GO:0015520 tetracycline:hydrogen antiporter activit...        36           6     2.14              32 0.01804 0.99231 0.01804 0.01804
28  GO:0042895             antibiotic transporter activity        36           6     2.14              33 0.01804 0.99231 0.01804 1.00000
29  GO:0000252 C-3 sterol dehydrogenase (C-4 sterol dec...        10           3     0.59              34 0.01825 0.39626 0.01825 0.01825
30  GO:0000253            3-keto sterol reductase activity        10           3     0.59              35 0.01825 0.39626 0.01825 0.01825
31  GO:0004495                mevaldate reductase activity        10           3     0.59              36 0.01825 0.39626 0.01825 0.01825
32  GO:0018451              epoxide dehydrogenase activity        10           3     0.59              37 0.01825 0.39626 0.01825 0.01825
33  GO:0018452 5-exo-hydroxycamphor dehydrogenase activ...        10           3     0.59              38 0.01825 0.39626 0.01825 0.01825
34  GO:0018453 2-hydroxytetrahydrofuran dehydrogenase a...        10           3     0.59              39 0.01825 0.39626 0.01825 0.01825
35  GO:0048258            3-ketoglucose-reductase activity        10           3     0.59              40 0.01825 0.39626 0.01825 0.01825
36  GO:0005543                       phospholipid binding         4           2     0.24              41 0.01950 0.99525 0.01950 0.01950
37  GO:0008240              tripeptidyl-peptidase activity         4           2     0.24              42 0.01950 0.87430 0.01950 1.00000
38  GO:0008418 protein N-terminal asparagine amidohydro...         4           2     0.24              43 0.01950 0.85403 0.01950 1.00000
39  GO:0008759 UDP-3-O-[3-hydroxymyristoyl] N-acetylglu...         4           2     0.24              44 0.01950 0.85403 0.01950 0.01950
40  GO:0009017    succinylglutamate desuccinylase activity         4           2     0.24              45 0.01950 0.85403 0.01950 0.01950
```

41	GO:0017159	pantetheinase activity	4	2	0.24	46	0.01950	0.85403	0.01950	0.01950
42	GO:0018748	iprodione amidohydrolase activity	4	2	0.24	47	0.01950	0.85403	0.01950	0.01950
43	GO:0018749	(3,5-dichlorophenylurea)acetate amidohyd...	4	2	0.24	48	0.01950	0.85403	0.01950	0.01950
44	GO:0019131	tripeptidyl-peptidase I activity	4	2	0.24	49	0.01950	0.87430	0.01950	0.01950
45	GO:0047419	N-acetylgalactosamine-6-phosphate deacet...	4	2	0.24	50	0.01950	0.85403	0.01950	0.01950
46	GO:0015238	drug transporter activity	38	6	2.26	51	0.02316	0.98226	0.02316	1.00000
47	GO:0015298	solute:cation antiporter activity	38	6	2.26	52	0.02316	0.98226	0.02316	1.00000
48	GO:0015299	solute:hydrogen antiporter activity	38	6	2.26	53	0.02316	0.98226	0.02316	1.00000
49	GO:0015300	solute:solute antiporter activity	38	6	2.26	54	0.02316	0.98226	0.02316	1.00000
50	GO:0004091	carboxylesterase activity	20	4	1.19	55	0.02783	0.27913	0.02783	0.02783
51	GO:0004650	polygalacturonase activity	21	4	1.25	57	0.03282	0.92052	0.03282	0.03282
52	GO:0016229	steroid dehydrogenase activity	21	4	1.25	58	0.03282	0.11273	0.03282	0.03282
53	GO:0003824	catalytic activity	3853	253	228.99	4	0.00179	8e-06	0.03464	0.84946
54	GO:0008875	gluconate dehydrogenase activity	13	3	0.77	59	0.03812	0.44410	0.03812	0.03812
55	GO:0015297	antiporter activity	43	6	2.56	60	0.03997	0.85300	0.03997	1.00000
56	GO:0000036	acyl carrier activity	6	2	0.36	61	0.04504	0.99738	0.04504	0.04504
57	GO:0000810	diacylglycerol pyrophosphate phosphatase...	6	2	0.36	62	0.04504	0.25444	0.04504	0.04504
58	GO:0004054	arginine kinase activity	6	2	0.36	63	0.04504	0.56756	0.04504	1.00000
59	GO:0004407	histone deacetylase activity	6	2	0.36	64	0.04504	0.67146	0.04504	0.04504
60	GO:0004551	nucleotide diphosphatase activity	6	2	0.36	65	0.04504	0.25444	0.04504	1.00000
61	GO:0004787	thiamin-pyrophosphatase activity	6	2	0.36	66	0.04504	0.25444	0.04504	0.04504
62	GO:0008758	UDP-2,3-diacylglucosamine hydrolase acti...	6	2	0.36	67	0.04504	0.25444	0.04504	0.04504
63	GO:0008796	bis(5’-nucleosyl)-tetraphosphatase activ...	6	2	0.36	68	0.04504	0.25444	0.04504	0.04504
64	GO:0008828	dATP pyrophosphohydrolase activity	6	2	0.36	69	0.04504	0.25444	0.04504	0.04504
65	GO:0018110	histone arginine kinase activity	6	2	0.36	70	0.04504	0.56756	0.04504	0.04504
66	GO:0019176	dihydroneopterin monophosphate phosphata...	6	2	0.36	71	0.04504	0.25444	0.04504	0.04504
67	GO:0019177	dihydroneopterin triphosphate pyrophosph...	6	2	0.36	72	0.04504	0.25444	0.04504	0.04504
68	GO:0035173	histone kinase activity	6	2	0.36	73	0.04504	0.56756	0.04504	1.00000
69	GO:0016863	intramolecular oxidoreductase activity, ...	14	3	0.83	74	0.04644	0.62172	0.04644	0.04644
70	GO:0050381	unspecific monooxygenase activity	45	6	2.67	75	0.04841	0.40667	0.04841	0.04841
71	GO:0008171	O-methyltransferase activity	34	5	2.02	76	0.04842	0.75897	0.04842	0.04842

########## Cellular component #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005835	fatty acid synthase complex	5	2	0.23	1	0.020	0.96056	0.020	0.020
2	GO:0016021	integral to membrane	698	42	32.79	2	0.033	0.06510	0.033	0.258
3	GO:0031224	intrinsic to membrane	698	42	32.79	3	0.033	0.06510	0.033	0.042

########## Biological process #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0006118	electron transport	599	57	35.90	1	0.00017	0.01914	0.00017	0.00017
2	GO:0006631	fatty acid metabolic process	82	11	4.92	3	0.00913	0.92800	0.00913	0.00913
3	GO:0006633	fatty acid biosynthetic process	64	9	3.84	5	0.01316	0.99177	0.01316	0.38507
4	GO:0016053	organic acid biosynthetic process	65	9	3.90	6	0.01450	0.98940	0.01450	1.00000
5	GO:0046394	carboxylic acid biosynthetic process	65	9	3.90	7	0.01450	0.98940	0.01450	0.48754
6	GO:0015904	tetracycline transport	36	6	2.16	8	0.01867	0.98096	0.01867	0.01867
7	GO:0015893	drug transport	38	6	2.28	10	0.02395	0.93576	0.02395	1.00000
8	GO:0042493	response to drug	50	7	3.00	11	0.02804	0.63170	0.02804	0.54763
9	GO:0006777	Mo-molybdopterin cofactor biosynthetic p...	5	2	0.30	14	0.03173	0.75800	0.03173	0.03173
10	GO:0019720	Mo-molybdopterin cofactor metabolic proc...	5	2	0.30	15	0.03173	0.75800	0.03173	1.00000
11	GO:0032324	molybdopterin cofactor biosynthetic proc...	5	2	0.30	16	0.03173	0.75800	0.03173	1.00000

12	GO:0042558	pteridine and derivative metabolic proce...	5	2	0.30	17	0.03173	0.75800	0.03173	1.00000
13	GO:0042559	pteridine and derivative biosynthetic pr...	5	2	0.30	18	0.03173	0.75800	0.03173	1.00000
14	GO:0043545	molybdopterin cofactor metabolic process	5	2	0.30	19	0.03173	0.75800	0.03173	1.00000
15	GO:0008610	lipid biosynthetic process	111	12	6.65	20	0.03263	0.90656	0.03263	1.00000

E.1.9 Imprint category E3

GO term over-representation results for category E3 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############
```

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0004043	L-aminoadipate-semialdehyde dehydrogenas...	14	4	0.34	1	0.00028	0.99974	0.00028	0.00028
2	GO:0008270	zinc ion binding	649	29	15.82	2	0.00077	0.03995	0.00077	0.00077
3	GO:0031177	phosphopantetheine binding	64	6	1.56	6	0.00442	0.60164	0.00442	0.00442
4	GO:0004316	3-oxoacyl-[acyl-carrier-protein] reducta...	18	3	0.44	10	0.00884	0.77232	0.00884	1.00000
5	GO:0003700	transcription factor activity	324	15	7.90	14	0.01189	0.18967	0.01189	0.01189
6	GO:0004497	monooxygenase activity	241	12	5.87	15	0.01407	0.02085	0.01407	0.07444
7	GO:0048037	cofactor binding	160	9	3.90	16	0.01572	0.03761	0.01572	0.04397
8	GO:0004517	nitric-oxide synthase activity	1	1	0.02	17	0.02438	0.99922	0.02438	0.02438
9	GO:0004584	dolichyl-phosphate-mannose-glycolipid al...	1	1	0.02	18	0.02438	0.99988	0.02438	0.02438
10	GO:0008116	prostaglandin-I synthase activity	1	1	0.02	19	0.02438	0.99932	0.02438	0.02438
11	GO:0016937	short-branched-chain-acyl-CoA dehydrogen...	1	1	0.02	20	0.02438	0.99998	0.02438	0.02438
12	GO:0017099	very-long-chain-acyl-CoA dehydrogenase a...	1	1	0.02	21	0.02438	0.99998	0.02438	0.02438
13	GO:0019109	acyl-CoA reductase activity	1	1	0.02	22	0.02438	0.99998	0.02438	0.02438
14	GO:0030528	transcription regulator activity	359	15	8.75	23	0.02760	0.13087	0.02760	0.76728
15	GO:0016646	oxidoreductase activity, acting on the C...	11	2	0.27	24	0.02809	0.84461	0.02809	0.02809
16	GO:0003677	DNA binding	664	24	16.19	25	0.02972	0.16640	0.02972	0.43615
17	GO:0003904	deoxyribodipyrimidine photo-lyase activi...	2	1	0.05	26	0.04816	0.69132	0.04816	0.04816
18	GO:0003913	DNA photolyase activity	2	1	0.05	27	0.04816	0.69132	0.04816	1.00000
19	GO:0004099	chitin deacetylase activity	2	1	0.05	28	0.04816	0.67360	0.04816	0.04816
20	GO:0004146	dihydrofolate reductase activity	2	1	0.05	29	0.04816	0.99990	0.04816	1.00000
21	GO:0004363	glutathione synthase activity	2	1	0.05	30	0.04816	0.80487	0.04816	0.04816
22	GO:0005267	potassium channel activity	2	1	0.05	31	0.04816	0.99954	0.04816	0.04816
23	GO:0008488	gamma-glutamyl carboxylase activity	2	1	0.05	32	0.04816	0.99860	0.04816	0.04816
24	GO:0008694	3-octaprenyl-4-hydroxybenzoate carboxy-l...	2	1	0.05	33	0.04816	0.99860	0.04816	0.04816
25	GO:0008710	8-amino-7-oxononanoate synthase activity	2	1	0.05	34	0.04816	0.99995	0.04816	0.04816
26	GO:0009042	valine-pyruvate transaminase activity	2	1	0.05	35	0.04816	0.37459	0.04816	0.04816
27	GO:0009045	xylose isomerase activity	2	1	0.05	36	0.04816	0.99941	0.04816	0.04816
28	GO:0016443	bidentate ribonuclease III activity	2	1	0.05	37	0.04816	0.50804	0.04816	0.04816
29	GO:0018790	2,3-dihydroxybenzoate decarboxylase acti...	2	1	0.05	38	0.04816	0.99860	0.04816	0.04816
30	GO:0018791	2-hydroxy-3-carboxy-6-oxo-7-methylocta-2...	2	1	0.05	39	0.04816	0.99860	0.04816	0.04816
31	GO:0018792	bis(4-chlorophenyl)acetate decarboxylase...	2	1	0.05	40	0.04816	0.99860	0.04816	0.04816
32	GO:0018793	3,5-dibromo-4-hydroxybenzoate decarboxyl...	2	1	0.05	41	0.04816	0.99860	0.04816	0.04816
33	GO:0018794	2-hydroxyisobutyrate decarboxylase activ...	2	1	0.05	42	0.04816	0.99860	0.04816	0.04816
34	GO:0018795	2-hydroxy-2-methyl-1,3-dicarbonate decar...	2	1	0.05	43	0.04816	0.99860	0.04816	0.04816
35	GO:0019167	3-octaprenyl-4-hydroxybenzoate decarboxy...	2	1	0.05	44	0.04816	0.99860	0.04816	0.04816
36	GO:0030755	quercetin 3-O-methyltransferase activity	2	1	0.05	45	0.04816	0.99783	0.04816	0.04816
37	GO:0016491	oxidoreductase activity	1146	41	27.94	7	0.00474	0.01060	0.04934	0.89819

```
##########  Cellular component  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0005634                                 nucleus       695          23    13.78               1  0.0031 0.00013 0.0031 0.0031
2   GO:0005960                  glycine cleavage complex         2           1     0.04               4  0.0393 1.00000 0.0393 0.0393

##########  Biological process  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0006118                       electron transport       599          23    14.08               1   0.011  0.0025 0.011  0.011
2   GO:0006544                 glycine metabolic process         8           2     0.19               2   0.014  1.0000 0.014  0.014
3   GO:0006350                           transcription       517          20    12.15               3   0.016  0.0153 0.016  0.184
4   GO:0006545              glycine biosynthetic process         1           1     0.02               4   0.024  1.0000 0.024  1.000
5   GO:0006809         nitric oxide biosynthetic process         1           1     0.02               5   0.024  0.9992 0.024  0.024
6   GO:0046209            nitric oxide metabolic process         1           1     0.02               6   0.024  0.9992 0.024  1.000
7   GO:0006355 regulation of transcription, DNA-depende...       395          15    9.28               7   0.042  0.1914 0.042  0.042
8   GO:0016559                       peroxisome fission         2           1     0.05               8   0.046  0.9478 0.046  0.046
9   GO:0048285                        organelle fission         2           1     0.05               9   0.046  0.9478 0.046  1.000
```

E.1.10 Imprint category E4

GO term over-representation results for category E4 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic     KS   elim  weight
1   GO:0008270                          zinc ion binding       649          18     8.55               6 0.00148 0.0276 0.0015 1.00000
2   GO:0003700           transcription factor activity       324          11     4.27               7 0.00313 0.1670 0.0031 0.00313
3   GO:0016491                oxidoreductase activity      1146          27    15.09               5 0.00093 0.0102 0.0084 0.18568
4   GO:0016705 oxidoreductase activity, acting on paire...       139           6     1.83               9 0.00959 0.0352 0.0096 1.00000
5   GO:0016216           isopenicillin-N synthase activity        13           2     0.17              10 0.01215 0.4330 0.0121 0.01215
6   GO:0046992 oxidoreductase activity, acting on X-H a...        13           2     0.17              11 0.01215 0.4330 0.0121 1.00000
7   GO:0046993 oxidoreductase activity, acting on X-H a...        13           2     0.17              12 0.01215 0.4330 0.0121 1.00000
8   GO:0050381           unspecific monooxygenase activity        45           3     0.59              13 0.02094 0.2667 0.0209 0.02094
9   GO:0016712 oxidoreductase activity, acting on paire...        48           3     0.63              14 0.02482 0.2210 0.0248 1.00000
10  GO:0016628 oxidoreductase activity, acting on the C...        19           2     0.25              15 0.02531 0.2602 0.0253 0.02531
11  GO:0004148        dihydrolipoyl dehydrogenase activity         2           1     0.03              16 0.02616 0.9045 0.0262 0.02616
12  GO:0008119     thiopurine S-methyltransferase activity         2           1     0.03              17 0.02616 0.9999 0.0262 0.02616
13  GO:0047927          gibberellin-44 dioxygenase activity         2           1     0.03              18 0.02616 0.5465 0.0262 0.02616
14  GO:0018585                   fluorene oxygenase activity        22           2     0.29              19 0.03334 0.0615 0.0333 0.03334
15  GO:0018586           mono-butyltin dioxygenase activity        22           2     0.29              20 0.03334 0.0615 0.0333 0.03334
16  GO:0018587            limonene 8-monooxygenase activity        22           2     0.29              21 0.03334 0.0615 0.0333 0.03334
17  GO:0018588          tri-n-butyltin dioxygenase activity        22           2     0.29              22 0.03334 0.0615 0.0333 0.03334
18  GO:0018589           di-n-butyltin dioxygenase activity        22           2     0.29              23 0.03334 0.0615 0.0333 0.03334
19  GO:0018590      methylsilanetriol hydroxylase activity        22           2     0.29              24 0.03334 0.0615 0.0333 0.03334
20  GO:0018591 methyl tertiary butyl ether 3-monooxygen...        22           2     0.29              25 0.03334 0.0615 0.0333 0.03334
21  GO:0018592    4-nitrocatechol 4-monooxygenase activity        22           2     0.29              26 0.03334 0.0615 0.0333 0.03334
22  GO:0018593 4-chlorophenoxyacetate monooxygenase act...        22           2     0.29              27 0.03334 0.0615 0.0333 0.03334
23  GO:0018594 tert-butyl alcohol 2-monooxygenase activ...        22           2     0.29              28 0.03334 0.0615 0.0333 0.03334
24  GO:0018595          alpha-pinene monooxygenase activity        22           2     0.29              29 0.03334 0.0615 0.0333 0.03334
```

```
25  GO:0018596     dimethylsilanediol hydroxylase activity        22           2     0.29              30 0.03334 0.0615 0.0333 0.03334
26  GO:0018597               ammonia monooxygenase activity        22           2     0.29              31 0.03334 0.0615 0.0333 0.03334
27  GO:0018598 hydroxymethylsilanetriol oxidase activit...        22           2     0.29              32 0.03334 0.0615 0.0333 0.03334
28  GO:0018599 2-hydroxyisobutyrate 3-monooxygenase act...        22           2     0.29              33 0.03334 0.0615 0.0333 0.03334
29  GO:0018600         alpha-pinene dehydrogenase activity        22           2     0.29              34 0.03334 0.0615 0.0333 0.03334
30  GO:0018601      4-nitrophenol 2-monooxygenase activity        22           2     0.29              35 0.03334 0.0615 0.0333 0.03334
31  GO:0004497                      monooxygenase activity       241           7     3.17              36 0.03831 0.0084 0.0383 1.00000
32  GO:0004321            fatty-acyl-CoA synthase activity         3           1     0.04              37 0.03899 0.8236 0.0390 0.03899
33  GO:0008840       dihydrodipicolinate synthase activity         3           1     0.04              38 0.03899 0.9212 0.0390 0.03899
34  GO:0019113             limonene monooxygenase activity        26           2     0.34              39 0.04535 0.1568 0.0454 1.00000

##########  Cellular component  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0005622                           intracellular      1314          19    13.59              1   0.018 0.00034 0.018  0.251
2   GO:0005634                                 nucleus       695          12     7.19              2   0.030 0.00011 0.030  0.030

##########  Biological process  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0006118                      electron transport       599          15     6.84              1  0.0022  0.0031 0.0022 0.0022
2   GO:0006355 regulation of transcription, DNA-depende...       395          11     4.51              2  0.0043  0.1915 0.0043 0.0043
3   GO:0017000             antibiotic biosynthetic process        15           2     0.17             12  0.0122  0.2360 0.0122 0.0122
4   GO:0016999                antibiotic metabolic process        16           2     0.18             14  0.0139  0.1304 0.0139 1.0000
5   GO:0017144                     drug metabolic process        16           2     0.18             15  0.0139  0.1304 0.0139 1.0000
6   GO:0006817                        phosphate transport         4           1     0.05             18  0.0449  0.7390 0.0449 0.0449
```


E.1.11 Imprint category E5

GO term over-representation results for category E5 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0003824                          catalytic activity      3853          23    17.14              1   0.006 1.3e-08 0.006  0.230
2   GO:0030060             L-malate dehydrogenase activity         3           1     0.01              2   0.013 0.99996 0.013  0.013
3   GO:0004069             aspartate transaminase activity         4           1     0.02              3   0.018 0.95545 0.018  0.018
4   GO:0004523                    ribonuclease H activity         4           1     0.02              4   0.018 0.94396 0.018  0.018
5   GO:0008800                    beta-lactamase activity         4           1     0.02              5   0.018 0.89366 0.018  0.018
6   GO:0016615               malate dehydrogenase activity         5           1     0.02              6   0.022 0.99994 0.022  1.000
7   GO:0045551     cinnamyl-alcohol dehydrogenase activity         5           1     0.02              7   0.022 0.99996 0.022  0.022
8   GO:0004301                  epoxide hydrolase activity         7           1     0.03              8   0.031 0.31503 0.031  0.031
9   GO:0004463           leukotriene-A4 hydrolase activity         7           1     0.03              9   0.031 0.31503 0.031  1.000
10  GO:0016803                    ether hydrolase activity         7           1     0.03             10   0.031 0.31503 0.031  1.000
11  GO:0031177                 phosphopantetheine binding        64           2     0.28             11   0.032 0.41264 0.032  0.032
12  GO:0016801 hydrolase activity, acting on ether bond...         8           1     0.04             12   0.035 0.53433 0.035  1.000
13  GO:0019842                           vitamin binding        78           2     0.35             13   0.046 0.19588 0.046  1.000
14  GO:0003990            acetylcholinesterase activity        11           1     0.05             14   0.048 0.18319 0.048  0.048
15  GO:0016207           4-coumarate-CoA ligase activity        11           1     0.05             15   0.048 0.39768 0.048  0.048
16  GO:0016812 hydrolase activity, acting on carbon-nit...        11           1     0.05             16   0.048 0.74014 0.048  1.000
```

```
        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0005792                               microsome         4           1     0.01              1  0.0086  0.3325 0.0086 0.0086
2   GO:0005576                 extracellular region        25           1     0.05              5  0.0528  0.7749 0.0528 0.0528
3   GO:0016020                              membrane      1079           4     2.33              6  0.1466  0.2554 0.1466 0.1898
4   GO:0016021                integral to membrane       698           2     1.50              7  0.4736  0.0049 0.4736 0.4736
5   GO:0031224              intrinsic to membrane       698           2     1.50              8  0.4736  0.0049 0.4736 1.0000

##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0009636                    response to toxin         3           1     0.01              1   0.014  0.6659 0.014  0.014
2   GO:0006108           malate metabolic process         5           1     0.02              2   0.022  1.0000 0.022  0.022
3   GO:0006100 tricarboxylic acid cycle intermediate me...         7           1     0.03              3   0.031  0.9999 0.031  1.000
4   GO:0007155                       cell adhesion         7           1     0.03              4   0.031  0.9065 0.031  0.031
5   GO:0022610                 biological adhesion         7           1     0.03              5   0.031  0.9065 0.031  1.000
6   GO:0043648         dicarboxylic acid metabolic process         7           1     0.03              6   0.031  0.9961 0.031  1.000
```

E.1.12 Imprint category E6

GO term over-representation results for category E6 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0004587    ornithine-oxo-acid transaminase activity         2           1     0.01              1   0.006 0.94064 0.006  0.006
2  GO:0030599                     pectinesterase activity         4           1     0.01              2   0.012 0.96142 0.012  0.012
3  GO:0045551     cinnamyl-alcohol dehydrogenase activity         5           1     0.02              3   0.015 0.86183 0.015  0.015
4  GO:0008451               X-Pro aminopeptidase activity         7           1     0.02              4   0.021 0.62758 0.021  0.021
5  GO:0019842                           vitamin binding        78           2     0.24              5   0.023 0.29827 0.023  0.023
6  GO:0016789         carboxylic ester hydrolase activity        79           2     0.24              6   0.023 0.15611 0.023  1.000
7  GO:0004525                  ribonuclease III activity         9           1     0.03              7   0.027 0.20792 0.027  0.027
8  GO:0003990               acetylcholinesterase activity        11           1     0.03              8   0.033 0.46562 0.033  0.033
9  GO:0030170                 pyridoxal phosphate binding        12           1     0.04              9   0.036 0.31559 0.036  1.000
10 GO:0016891 endoribonuclease activity, producing 5'-...        16           1     0.05             10   0.047 0.49723 0.047  1.000
11 GO:0008233                          peptidase activity       278           3     0.84             11   0.049 0.25051 0.049  1.000

##########  Cellular component  #############

       GO.ID                                  Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0005618                            cell wall         8           1     0.01              1   0.014  0.5276 0.014  0.014
2  GO:0030312       external encapsulating structure        14           1     0.02              2   0.024  0.7099 0.024  1.000
3  GO:0005634                              nucleus       695           2     1.20              3   0.348 1.7e-05 0.348  0.348
4  GO:0043227               membrane-bound organelle       824           2     1.42              4   0.446 1.1e-05 0.446  1.000
5  GO:0043231 intracellular membrane-bound organelle       824           2     1.42              5   0.446 1.1e-05 0.446  1.000

##########  Biological process  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0042545                cell wall modification         4           1     0.01              1  0.0086 0.95071 0.0086 0.0086
```

```
2  GO:0006508                              proteolysis       271           3     0.58               4  0.0174 0.09097 0.0174 0.0174
3  GO:0016998                cell wall catabolic process        10           1     0.02               5  0.0214 0.16018 0.0214 0.0214
```

E.1.13 Imprint category E7

GO term over-representation results for category E7 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS   elim weight
1  GO:0016631 enoyl-[acyl-carrier-protein] reductase a...         5           1     0.00               1  0.0036 0.987 0.0036 0.0036
2  GO:0018498 2,3-dihydroxy-2,3-dihydro-phenylpropiona...         5           1     0.00               2  0.0036 0.987 0.0036 0.0036
3  GO:0018499 cis-2,3-dihydrodiol DDT dehydrogenase ac...         5           1     0.00               3  0.0036 0.987 0.0036 0.0036
4  GO:0018500 trans-9R,10R-dihydrodiolphenanthrene deh...         5           1     0.00               4  0.0036 0.987 0.0036 0.0036
5  GO:0018501 cis-chlorobenzene dihydrodiol dehydrogen...         5           1     0.00               5  0.0036 0.987 0.0036 0.0036
6  GO:0018502 2,5-dichloro-2,5-cyclohexadiene-1,4-diol...         5           1     0.00               6  0.0036 0.987 0.0036 0.0036
7  GO:0018503 trans-1,2-dihydrodiolphenanthrene dehydr...         5           1     0.00               7  0.0036 0.987 0.0036 0.0036
8  GO:0004672                      protein kinase activity       222           2     0.16               8  0.0088 0.889 0.0088 1.0000
9  GO:0004682                 protein kinase CK2 activity        33           1     0.02              12  0.0233 0.090 0.0233 0.0233
10 GO:0004691      cAMP-dependent protein kinase activity        33           1     0.02              13  0.0233 0.090 0.0233 0.0233
11 GO:0008605       protein kinase CK2 regulator activity        34           1     0.02              14  0.0240 0.156 0.0240 0.0240
12 GO:0008603 cAMP-dependent protein kinase regulator ...        35           1     0.02              15  0.0247 0.250 0.0247 0.0247
13 GO:0004680                       casein kinase activity        55           1     0.04              18  0.0386 0.021 0.0386 1.0000
14 GO:0004690 cyclic nucleotide-dependent protein kina...        55           1     0.04              19  0.0386 0.021 0.0386 1.0000
15 GO:0019207                    kinase regulator activity        58           1     0.04              20  0.0407 0.064 0.0407 1.0000
16 GO:0019887           protein kinase regulator activity        58           1     0.04              21  0.0407 0.064 0.0407 1.0000

##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0005956                  protein kinase CK2 complex        34           1     0.01               1   0.015   0.050 0.015  0.015
2  GO:0005952       cAMP-dependent protein kinase complex        35           1     0.02               2   0.015   0.090 0.015  0.015
3  GO:0043234                             protein complex       475           1     0.20               3   0.205   0.063 0.205  1.000

##########  Biological process  #############

        GO.ID                                   Term Annotated Significant Expected Rank in classic classic     KS   elim weight
1  GO:0006468       protein amino acid phosphorylation       198           2     0.13               1  0.0053 0.6796 0.0053 0.0053
```

E.1.14 Imprint category E8

GO term over-representation results for category E8 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS  elim weight
```

```
1  GO:0004682                protein kinase CK2 activity        33           1     0.02              1   0.023 0.153 0.023  0.023
2  GO:0004691      cAMP-dependent protein kinase activity        33           1     0.02              2   0.023 0.153 0.023  0.023
3  GO:0008605       protein kinase CK2 regulator activity        34           1     0.02              3   0.024 0.263 0.024  0.024
4  GO:0008603 cAMP-dependent protein kinase regulator ...        35           1     0.02              4   0.025 0.250 0.025  0.025
5  GO:0004680                      casein kinase activity        55           1     0.04              5   0.039 0.021 0.039  1.000
6  GO:0004690 cyclic nucleotide-dependent protein kina...        55           1     0.04              6   0.039 0.021 0.039  1.000
7  GO:0019207                   kinase regulator activity        58           1     0.04              7   0.041 0.064 0.041  1.000
8  GO:0019887           protein kinase regulator activity        58           1     0.04              8   0.041 0.064 0.041  1.000

##########  Cellular component  #############

        GO.ID                                  Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0005956             protein kinase CK2 complex        34           1     0.03              1   0.029 0.10690 0.029  0.029
2  GO:0005952  cAMP-dependent protein kinase complex        35           1     0.03              2   0.030 0.11170 0.030  0.030

##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0009116                nucleoside metabolic process        19           1     0.02              1   0.016 0.07062 0.016  0.016
```

E.1.15 Imprint category E9

GO term over-representation results for category E9 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0004672                     protein kinase activity       222           1     0.04              1   0.040  0.8760 0.040  0.040
2  GO:0016773 phosphotransferase activity, alcohol gro...       265           1     0.05              2   0.047  0.8377 0.047  1.000

##########  Cellular component  #############

        GO.ID                                  Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0005956             protein kinase CK2 complex        34           0        0              1   0.029  0.0497 0.029  0.029
2  GO:0005952  cAMP-dependent protein kinase complex        35           0        0              2   0.030  0.0530 0.030  0.030

##########  Biological process  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic     KS  elim weight
1  GO:0006468       protein amino acid phosphorylation       198           1     0.04              1   0.043 0.5956 0.043  0.043
```

E.1.16 Imprint category E10

GO term over-representation results for category E10 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############
```

```
        GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0004289                      subtilase activity        18           1     0.00               1  0.0032   0.295 0.0032 0.0032

##########  Cellular component  #############

        GO.ID                                Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0005956            protein kinase CK2 complex        34           0        0               1   0.029  0.0497 0.029  0.029
2  GO:0005952 cAMP-dependent protein kinase complex        35           0        0               2   0.030  0.0530 0.030  0.030

##########  Biological process  #############

        GO.ID                                    Term Annotated Significant Expected Rank in classic classic     KS  elim weight
1  GO:0006508                            proteolysis       271           1     0.06               1   0.058 0.0969 0.058  0.058
```

E.1.17 Imprint categories E5–10 combined

GO term over-representation results for the combined categories E5–E10 of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

         GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS    elim  weight
1   GO:0045551     cinnamyl-alcohol dehydrogenase activity         5           2     0.05               2 0.00082  1.0000 0.00082 0.00082
2   GO:0003824                         catalytic activity      3853          46    35.65               1 0.00073 2.6e-08 0.00321 0.35936
3   GO:0003990               acetylcholinesterase activity        11           2     0.10               3 0.00438  0.4548 0.00438 0.00438
4   GO:0019842                           vitamin binding        78           4     0.72               4 0.00561  0.3752 0.00561 0.00561
5   GO:0016891 endoribonuclease activity, producing 5'-...        16           2     0.15               5 0.00928  0.4897 0.00928 0.00928
6   GO:0003960            NADPH:quinone reductase activity        17           2     0.16               6 0.01045  0.0013 0.01045 0.01045
7   GO:0004672                     protein kinase activity       222           6     2.05              10 0.01584  0.9322 0.01584 0.06741
8   GO:0001584            rhodopsin-like receptor activity        22           2     0.20              11 0.01723  0.1953 0.01723 0.01723
9   GO:0004587    ornithine-oxo-acid transaminase activity         2           1     0.02              12 0.01842  0.9373 0.01842 0.01842
10  GO:0031177                 phosphopantetheine binding        64           3     0.59              13 0.02094  0.5311 0.02094 1.00000
11  GO:0004930        G-protein coupled receptor activity        25           2     0.23              14 0.02199  0.0782 0.02199 1.00000
12  GO:0016655 oxidoreductase activity, acting on NADH ...        26           2     0.24              15 0.02369  0.0740 0.02369 1.00000
13  GO:0008483                      transaminase activity        28           2     0.26              16 0.02723  0.3991 0.02723 1.00000
14  GO:0030060            L-malate dehydrogenase activity         3           1     0.03              17 0.02751  0.9999 0.02751 0.02751
15  GO:0016773 phosphotransferase activity, alcohol gro...       265           6     2.45              18 0.03430  0.8842 0.03430 1.00000
16  GO:0004069            aspartate transaminase activity         4           1     0.04              20 0.03651  0.9525 0.03651 0.03651
17  GO:0004523                   ribonuclease H activity         4           1     0.04              21 0.03651  0.9417 0.03651 1.00000
18  GO:0008800                   beta-lactamase activity         4           1     0.04              22 0.03651  0.8912 0.03651 0.03651
19  GO:0030599                   pectinesterase activity         4           1     0.04              23 0.03651  0.9597 0.03651 0.03651
20  GO:0004682               protein kinase CK2 activity        33           2     0.31              24 0.03694  0.1558 0.03694 0.03694
21  GO:0004691     cAMP-dependent protein kinase activity        33           2     0.31              25 0.03694  0.1558 0.03694 0.03694
22  GO:0008171              O-methyltransferase activity        34           2     0.31              26 0.03902  0.4724 0.03902 0.03902
23  GO:0008605      protein kinase CK2 regulator activity        34           2     0.31              27 0.03902  0.2498 0.03902 0.03902
24  GO:0008603 cAMP-dependent protein kinase regulator ...        35           2     0.32              28 0.04114  0.3628 0.04114 0.04114
25  GO:0016615              malate dehydrogenase activity         5           1     0.05              32 0.04543  0.9998 0.04543 1.00000
26  GO:0016631 enoyl-[acyl-carrier-protein] reductase a...         5           1     0.05              33 0.04543  0.9821 0.04543 0.04543
27  GO:0018498 2,3-dihydroxy-2,3-dihydro-phenylpropiona...         5           1     0.05              34 0.04543  0.9821 0.04543 0.04543
28  GO:0018499 cis-2,3-dihydrodiol DDT dehydrogenase ac...         5           1     0.05              35 0.04543  0.9821 0.04543 0.04543
```

```
29  GO:0018500 trans-9R,10R-dihydrodiolphenanthrene deh...         5           1     0.05              36 0.04543  0.9821 0.04543 0.04543
30  GO:0018501 cis-chlorobenzene dihydrodiol dehydrogen...         5           1     0.05              37 0.04543  0.9821 0.04543 0.04543
31  GO:0018502 2,5-dichloro-2,5-cyclohexadiene-1,4-diol...         5           1     0.05              38 0.04543  0.9821 0.04543 0.04543
32  GO:0018503 trans-1,2-dihydrodiolphenanthrene dehydr...         5           1     0.05              39 0.04543  0.9821 0.04543 0.04543

##########  Cellular component  #############

        GO.ID                                Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0005956            protein kinase CK2 complex        34           2     0.18               1   0.013  0.0991 0.013  0.013
2  GO:0005952  cAMP-dependent protein kinase complex        35           2     0.18               2   0.013  0.1640 0.013  0.013
3  GO:0005792                             microsome         4           1     0.02               3   0.021  0.3291 0.021  0.021
4  GO:0042598                    vesicular fraction         4           1     0.02               4   0.021  0.3291 0.021  1.000
5  GO:0000267                         cell fraction         5           1     0.03               5   0.026  0.1673 0.026  1.000
6  GO:0005624                     membrane fraction         5           1     0.03               6   0.026  0.1673 0.026  1.000
7  GO:0005618                             cell wall         8           1     0.04               7   0.041  0.5232 0.041  0.041

##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0006468          protein amino acid phosphorylation       198           6     1.71               1  0.0064   0.732 0.0064 0.0064
2  GO:0009636                      response to toxin         3           1     0.03               5  0.0257   0.661 0.0257 0.0257
3  GO:0007166 cell surface receptor linked signal tran...        30           2     0.26               6  0.0271   0.088 0.0271 1.0000
4  GO:0007186 G-protein coupled receptor protein signa...        30           2     0.26               7  0.0271   0.088 0.0271 0.0271
5  GO:0042545                   cell wall modification         4           1     0.03               8  0.0341   0.948 0.0341 0.0341
6  GO:0006108                 malate metabolic process         5           1     0.04               9  0.0424   1.000 0.0424 0.0424
```


E.1.18 Imprint category F

GO term over-representation results for category F of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

    GO.ID                                  Term Annotated Significant Expected Rank in classic classic   KS  elim weight
1  GO:0003950        NAD+ ADP-ribosyltransferase activity         4           2     0.01               1   4e-05 0.41 4e-05  4e-05
2  GO:0004672                   protein kinase activity       222           3     0.59               4   0.019 0.87 0.019  0.019
3  GO:0016773 phosphotransferase activity, alcohol gro...       265           3     0.71               6   0.031 0.83 0.031  1.000
4  GO:0016301                          kinase activity       297           3     0.79               7   0.041 0.97 0.041  1.000

##########  Cellular component  #############

    GO.ID                                Term Annotated Significant Expected Rank in classic classic      KS elim weight
1  GO:0016021                integral to membrane       698           2     0.90               1    0.22  0.0047 0.22   0.22
2  GO:0031224               intrinsic to membrane       698           2     0.90               2    0.22  0.0047 0.22   1.00
3  GO:0044425                       membrane part       734           2     0.95               3    0.24  0.0135 0.24   1.00
4  GO:0016020                            membrane      1079           2     1.40               4    0.45  0.2030 0.45   1.00

##########  Biological process  #############

    GO.ID                                  Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0006468       protein amino acid phosphorylation       198           3     0.51               1   0.013  0.5919 0.013  0.013
```

```
2  GO:0009166             nucleotide catabolic process         5           1     0.01              2   0.013  0.3499 0.013  0.013
3  GO:0016310                          phosphorylation       247           3     0.64              3   0.023  0.8454 0.023  1.000
4  GO:0006793             phosphorus metabolic process       265           3     0.69              4   0.028  0.8860 0.028  1.000
5  GO:0006796              phosphate metabolic process       265           3     0.69              5   0.028  0.8860 0.028  1.000
```

E.1.19 Imprint category G

GO term over-representation results for category G of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0004329    formate-tetrahydrofolate ligase activity         1           1     0.00               1  0.0027 0.99999 0.0027 0.0027
2   GO:0004345 glucose-6-phosphate 1-dehydrogenase acti...         1           1     0.00               2  0.0027 1.00000 0.0027 0.0027
3   GO:0004139     deoxyribose-phosphate aldolase activity         2           1     0.01               3  0.0053 0.40228 0.0053 0.0053
4   GO:0017076                  purine nucleotide binding       759           6     2.03               4  0.0101 0.79857 0.0101 0.3321
5   GO:0000166                        nucleotide binding       785           6     2.10               5  0.0119 0.65538 0.0119 1.0000
6   GO:0005388        calcium-transporting ATPase activity         8           1     0.02               6  0.0212 0.85798 0.0212 0.0212
7   GO:0015085            calcium ion transporter activity         8           1     0.02               7  0.0212 0.85798 0.0212 1.0000
8   GO:0005525                               GTP binding        94           2     0.25               8  0.0252 0.89854 0.0252 0.0252
9   GO:0019001                  guanyl nucleotide binding        94           2     0.25               9  0.0252 0.89854 0.0252 1.0000
10  GO:0005515                            protein binding       125           2     0.33              11  0.0427 0.89203 0.0427 0.0427
11  GO:0003960            NADPH:quinone reductase activity        17           1     0.05              12  0.0445 0.00022 0.0445 0.0445
12  GO:0015082 di-, tri-valent inorganic cation transpo...        18           1     0.05              13  0.0470 0.71833 0.0470 1.0000

##########  Cellular component  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS elim weight
1   GO:0005737                                cytoplasm       418           1     0.72               1    0.55 0.96805 0.55   0.55

##########  Biological process  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0009264       deoxyribonucleotide catabolic process         2           1     0.00               1  0.0039  0.3965 0.0039 0.0039
2   GO:0006816                        calcium ion transport         7           1     0.01               3  0.0135  0.8993 0.0135 0.0135
3   GO:0009396 folic acid and derivative biosynthetic p...         7           1     0.01               4  0.0135  0.9930 0.0135 0.0135
4   GO:0006760 folic acid and derivative metabolic proc...         8           1     0.02               5  0.0154  0.9473 0.0154 1.0000
5   GO:0015674 di-, tri-valent inorganic cation transpo...        18           1     0.03               7  0.0344  0.6419 0.0344 1.0000
6   GO:0016192                  vesicle-mediated transport        23           1     0.04               8  0.0438  0.9459 0.0438 0.0438
```

E.1.20 Imprint category I

GO term over-representation results for category I of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############
```

```
         GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS    elim  weight
1   GO:0031177                  phosphopantetheine binding        64          13     4.07               3 0.00015 0.930 0.00015 0.00015
2   GO:0048037                          cofactor binding       160          23    10.16               4 0.00017 0.105 0.00017 0.00038
3   GO:0005524                               ATP binding       627          61    39.83               7 0.00034 0.995 0.00034 0.22610
4   GO:0003910                DNA ligase (ATP) activity        11           5     0.70               8 0.00034 0.854 0.00034 0.00034
5   GO:0042626 ATPase activity, coupled to transmembran...       148          19     9.40              13 0.00241 0.985 0.00241 0.53537
6   GO:0008270                          zinc ion binding       649          58    41.23              17 0.00373 0.169 0.00373 0.00373
7   GO:0016303      phosphatidylinositol 3-kinase activity         3           2     0.19              24 0.01157 0.678 0.01157 0.01157
8   GO:0003677                               DNA binding       664          55    42.18              27 0.02106 0.373 0.02106 0.02106
9   GO:0015662 ATPase activity, coupled to transmembran...        26           5     1.65              28 0.02186 0.973 0.02186 0.02186
10  GO:0005179                          hormone activity         4           2     0.25              29 0.02216 0.797 0.02216 0.02216
11  GO:0009975                          cyclase activity         4           2     0.25              30 0.02216 1.000 0.02216 0.06338
12  GO:0008484           sulfuric ester hydrolase activity        11           3     0.70              31 0.02861 0.783 0.02861 0.02861
13  GO:0005102                          receptor binding         5           2     0.32              32 0.03540 0.869 0.03540 1.00000
14  GO:0003700              transcription factor activity       324          29    20.58              33 0.03623 0.282 0.03623 0.47202
15  GO:0004344 glucose dehydrogenase (acceptor) activit...        12           3     0.76              34 0.03640 0.733 0.03640 0.03640
16  GO:0030528           transcription regulator activity       359          31    22.80              35 0.04706 0.265 0.04706 0.40128
17  GO:0016773 phosphotransferase activity, alcohol gro...       265          24    16.83              36 0.04793 0.890 0.04793 0.10848

##########  Cellular component  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0005634                                  nucleus       695          57    44.04               1   0.011 0.00152 0.011  0.012

##########  Biological process  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS    elim  weight
1   GO:0006633             fatty acid biosynthetic process        64          12     3.99               2 0.00048 0.998 0.00048 1.00000
2   GO:0006310                           DNA recombination        14           5     0.87               6 0.00114 0.533 0.00114 0.00114
3   GO:0006350                               transcription       517          47    32.21               7 0.00418 0.084 0.00418 0.10041
4   GO:0019219 regulation of nucleobase, nucleoside, nu...       410          37    25.55               8 0.01230 0.455 0.01230 0.03414
5   GO:0031323    regulation of cellular metabolic process       413          37    25.73               9 0.01373 0.464 0.01373 0.28510
6   GO:0009892    negative regulation of metabolic process         9           3     0.56              10 0.01518 1.000 0.01518 1.00000
7   GO:0031324 negative regulation of cellular metaboli...         9           3     0.56              11 0.01518 1.000 0.01518 1.00000
8   GO:0045934 negative regulation of nucleobase, nucle...         9           3     0.56              12 0.01518 1.000 0.01518 1.00000
9   GO:0019222             regulation of metabolic process       418          37    26.05              13 0.01641 0.500 0.01641 0.69900
10  GO:0032774                   RNA biosynthetic process       408          36    25.42              14 0.01868 0.373 0.01868 0.50500
11  GO:0045449                regulation of transcription       408          36    25.42              15 0.01868 0.373 0.01868 0.27798
12  GO:0006355 regulation of transcription, DNA-depende...       395          35    24.61              16 0.01915 0.403 0.01915 0.26932
13  GO:0050794             regulation of cellular process       437          38    27.23              18 0.01963 0.319 0.01963 0.72452
14  GO:0048523     negative regulation of cellular process        10           3     0.62              19 0.02070 1.000 0.02070 1.00000
15  GO:0050789           regulation of biological process       456          39    28.41              20 0.02318 0.305 0.02318 1.00000
16  GO:0006351               transcription, DNA-dependent       406          35    25.30              21 0.02780 0.299 0.02780 1.00000
17  GO:0048519 negative regulation of biological proces...        12           3     0.75              23 0.03460 1.000 0.03460 1.00000
18  GO:0006342                        chromatin silencing         6           2     0.37              24 0.04911 1.000 0.04911 0.04911
19  GO:0006636                  fatty acid desaturation           6           2     0.37              25 0.04911 0.996 0.04911 1.00000
20  GO:0006952                        defense response          6           2     0.37              26 0.04911 0.802 0.04911 0.04911
21  GO:0016458                          gene silencing          6           2     0.37              27 0.04911 1.000 0.04911 1.00000
22  GO:0031507                heterochromatin formation         6           2     0.37              28 0.04911 1.000 0.04911 1.00000
23  GO:0045814 negative regulation of gene expression, ...        6           2     0.37              29 0.04911 1.000 0.04911 1.00000
24  GO:0045892 negative regulation of transcription, DN...        6           2     0.37              30 0.04911 1.000 0.04911 1.00000
```

E.1.21 Imprint category J

GO term over-representation results for category J of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS   elim weight
1   GO:0004252          serine-type endopeptidase activity        39           6     1.55               1  0.0041 0.7311 0.0041 0.0041
2   GO:0008840       dihydrodipicolinate synthase activity         3           2     0.12               2  0.0046 0.9991 0.0046 0.0046
3   GO:0016491                    oxidoreductase activity      1146          62    45.68               3  0.0047 0.0063 0.0087 0.5746
4   GO:0003959               NADPH dehydrogenase activity         4           2     0.16               4  0.0090 0.5658 0.0090 0.0090
5   GO:0016216          isopenicillin-N synthase activity        13           3     0.52               6  0.0133 0.4815 0.0133 0.0133
6   GO:0046992 oxidoreductase activity, acting on X-H a...        13           3     0.52               7  0.0133 0.4815 0.0133 1.0000
7   GO:0046993 oxidoreductase activity, acting on X-H a...        13           3     0.52               8  0.0133 0.4815 0.0133 1.0000
8   GO:0003973         (S)-2-hydroxy-acid oxidase activity         6           2     0.24               9  0.0213 0.3389 0.0213 1.0000
9   GO:0008891                  glycolate oxidase activity         6           2     0.24              10  0.0213 0.3389 0.0213 0.0213
10  GO:0030693                           caspase activity         6           2     0.24              11  0.0213 0.7505 0.0213 0.0213
11  GO:0004029       aldehyde dehydrogenase (NAD) activity         7           2     0.28              12  0.0291 0.3273 0.0291 0.0291
12  GO:0008061                           chitin binding         7           2     0.28              13  0.0291 0.9663 0.0291 0.0291
13  GO:0018667        cyclohexanone monooxygenase activity         7           2     0.28              14  0.0291 0.9895 0.0291 0.0291
14  GO:0016899 oxidoreductase activity, acting on the C...        8           2     0.32              17  0.0378 0.2620 0.0378 1.0000
15  GO:0003997                  acyl-CoA oxidase activity         1           1     0.04              18  0.0399 0.9997 0.0399 0.0399
16  GO:0004107               chorismate synthase activity         1           1     0.04              19  0.0399 0.9987 0.0399 0.0399
17  GO:0004287             prolyl oligopeptidase activity         1           1     0.04              20  0.0399 0.9970 0.0399 1.0000
18  GO:0004350 glutamate-5-semialdehyde dehydrogenase a...        1           1     0.04              21  0.0399 1.0000 0.0399 0.0399
19  GO:0004479 methionyl-tRNA formyltransferase activit...        1           1     0.04              22  0.0399 0.9999 0.0399 0.0399
20  GO:0004622                  lysophospholipase activity         1           1     0.04              23  0.0399 0.9977 0.0399 0.0399
21  GO:0004731    purine-nucleoside phosphorylase activity         1           1     0.04              24  0.0399 1.0000 0.0399 0.0399
22  GO:0004896 hematopoietin/interferon-class (D200-dom...        1           1     0.04              25  0.0399 0.9971 0.0399 0.0399
23  GO:0004521                  endoribonuclease activity        21           3     0.84              26  0.0489 0.9534 0.0489 0.1045
24  GO:0016620 oxidoreductase activity, acting on the a...        35           4     1.40              27  0.0489 0.4210 0.0489 1.0000

##########  Cellular component  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0009339                   glycolate oxidase complex         6           2     0.22               1   0.018 0.24376 0.018  0.018
2   GO:0016021                        integral to membrane       698          35    25.87               2   0.021 0.05276 0.021  0.021
3   GO:0031224                      intrinsic to membrane       698          35    25.87               3   0.021 0.05276 0.021  0.397
4   GO:0044425                             membrane part       734          36    27.21               4   0.027 0.08871 0.027  0.733

##########  Biological process  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS  elim weight
1   GO:0017000             antibiotic biosynthetic process        15           3     0.60               1   0.021 0.2071 0.021  0.021
2   GO:0016999                antibiotic metabolic process        16           3     0.65               2   0.025 0.1266 0.025  1.000
3   GO:0017144                     drug metabolic process        16           3     0.65               3   0.025 0.1266 0.025  1.000
4   GO:0006635                fatty acid beta-oxidation         1           1     0.04               4   0.040 0.9996 0.040  0.040
5   GO:0009405                           pathogenesis         1           1     0.04               5   0.040 0.9979 0.040  0.040
6   GO:0019395                      fatty acid oxidation         1           1     0.04               6   0.040 0.9996 0.040  1.000
```

E.1.22 Imprint category K

GO term over-representation results for category K of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0005093     Rab GDP-dissociation inhibitor activity         1           1     0.00               1  0.0037  1.0000 0.0037 0.0037
2   GO:0004310 farnesyl-diphosphate farnesyltransferase...         2           1     0.01               2  0.0075  0.9415 0.0075 0.0075
3   GO:0004344 glucose dehydrogenase (acceptor) activit...        12           1     0.04               6  0.0440  0.7085 0.0440 0.0440
4   GO:0016216           isopenicillin-N synthase activity        13           1     0.05               7  0.0476  0.2536 0.0476 0.0476
5   GO:0046992 oxidoreductase activity, acting on X-H a...        13           1     0.05               8  0.0476  0.2536 0.0476 1.0000
6   GO:0046993 oxidoreductase activity, acting on X-H a...        13           1     0.05               9  0.0476  0.2536 0.0476 1.0000

##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS elim weight
1   GO:0016021                       integral to membrane       698           4     2.41               1    0.20 0.00672 0.20   0.20
2   GO:0031224                      intrinsic to membrane       698           4     2.41               2    0.20 0.00672 0.20   1.00
3   GO:0044425                            membrane part       734           4     2.53               3    0.22 0.01789 0.22   1.00
4   GO:0005634                                  nucleus       695           3     2.40               4    0.45 2.4e-05 0.45   0.45

##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0008610                 lipid biosynthetic process       111           3     0.43               1  0.0084 0.57889 0.0084 0.0084
2   GO:0043087              regulation of GTPase activity         6           1     0.02               3  0.0231 0.87449 0.0231 0.0231
3   GO:0051336           regulation of hydrolase activity         7           1     0.03               4  0.0269 0.57893 0.0269 1.0000
```

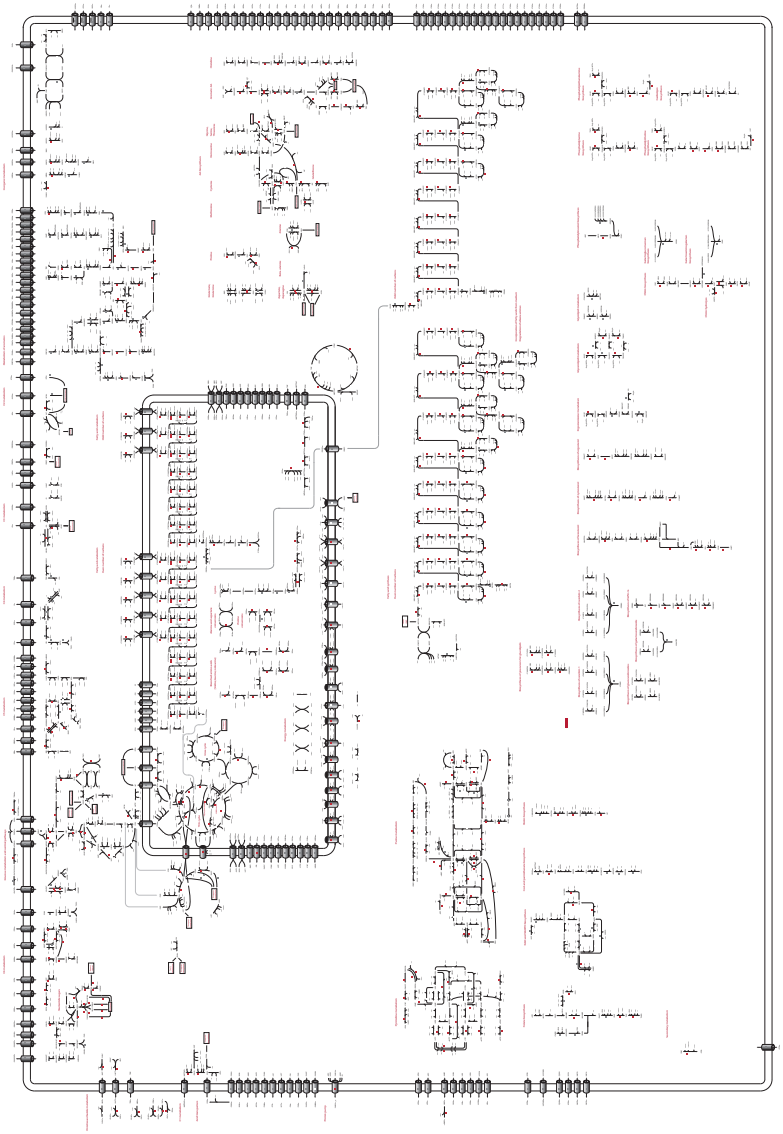
E.1.23 Imprint category L

GO term over-representation results for category L of table 7.2. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS    elim  weight
1   GO:0004563       beta-N-acetylhexosaminidase activity         4           2     0.00               1 1.1e-06 0.47821 1.1e-06 1.1e-06
2   GO:0004316 3-oxoacyl-[acyl-carrier-protein] reducta...        18           1     0.01               5  0.0096 0.32917  0.0096  0.0096

##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS elim weight
1   GO:0016021                       integral to membrane       698           0        0               1    0.20  0.0042 0.20   0.20

##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0005975             carbohydrate metabolic process       302           2     0.20               1   0.012 0.87510 0.012  0.012
```

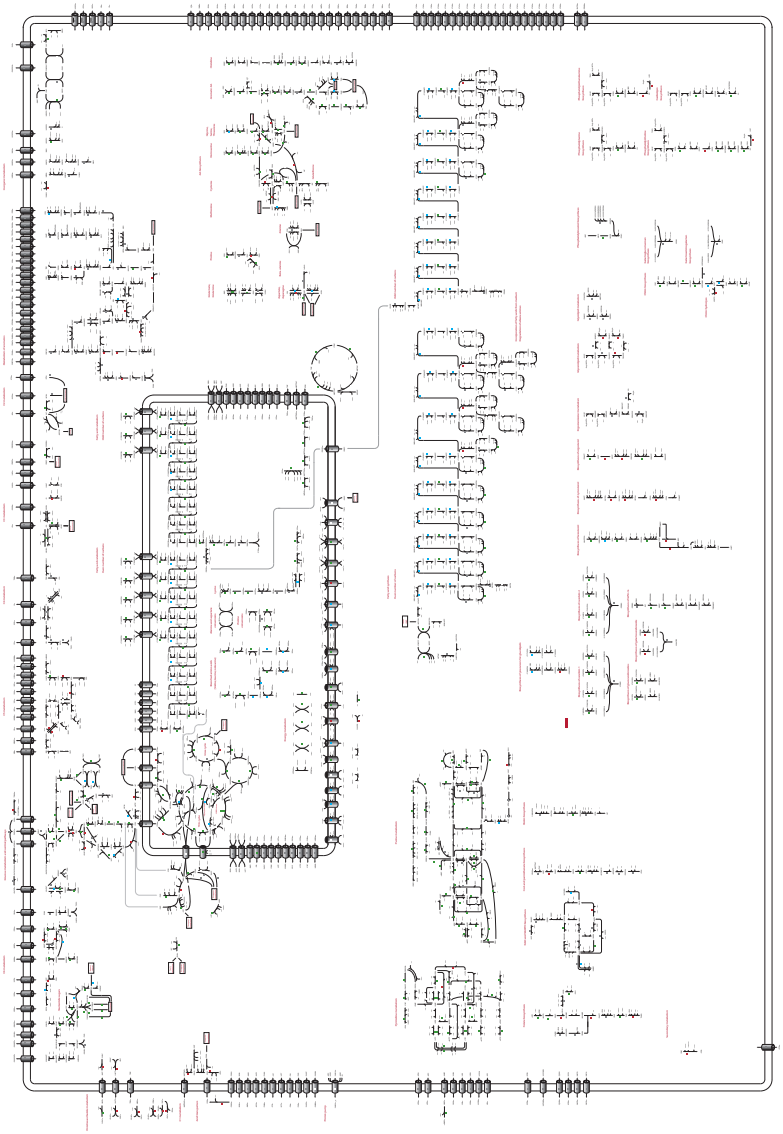
E.2 Overview of metabolic enzymes differing on an amino acid level

Red boxes denote genes with differences between *A. niger* CBS 513.88 and ATCC 1015. Gray boxes indicate that no gene for the reaction could be found. White boxes/No box indicate no difference between the strains.



E.3 Map of significantly regulated metabolism genes

Green boxes denote reactions where the corresponding genes are up-regulated in *A. niger* CBS 513.88. Red boxes show up-regulation in ATCC 1015. Blue boxes demonstrate that putative iso-enzymes exist that are up-regulated in each of the two strains. White boxes/No box indicate no significant change between the strains.



E.4 GO-term over-representation tables for transcriptome analysis

E.4.1 The 250 most up-regulated genes in *A. niger* CBS 513.88

GO term over-representation results for the 250 most up-regulated and statistically significantly changed genes in *A. niger* CBS 513.88 relative to *A. niger* ATCC 1015. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############
```

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0016838	carbon-oxygen lyase activity, acting on ...	5	4	0.15	4	3.3e-06	0.919	3.3e-06	3.3e-06
2	GO:0005524	ATP binding	627	38	18.19	5	5.7e-06	0.926	5.7e-06	5.7e-06
3	GO:0004812	aminoacyl-tRNA ligase activity	51	11	1.48	1	1.5e-07	1.000	2.3e-05	1.5e-07
4	GO:0046912	transferase activity, transferring acyl ...	13	4	0.38	10	0.00040	0.886	0.00040	0.00040
5	GO:0004055	argininosuccinate synthase activity	2	2	0.06	11	0.00084	0.997	0.00084	0.00084
6	GO:0004815	aspartate-tRNA ligase activity	8	3	0.23	12	0.00120	1.000	0.00120	1.00000
7	GO:0003849	3-deoxy-7-phosphoheptulonate synthase ac...	3	2	0.09	13	0.00246	1.000	0.00246	0.00246
8	GO:0004086	carbamoyl-phosphate synthase activity	3	2	0.09	14	0.00246	0.998	0.00246	0.00246
9	GO:0019904	protein domain specific binding	3	2	0.09	15	0.00246	1.000	0.00246	0.00246
10	GO:0005199	structural constituent of cell wall	4	2	0.12	16	0.00483	0.995	0.00483	0.00483
11	GO:0003855	3-dehydroquinate dehydratase activity	5	2	0.15	17	0.00789	0.597	0.00789	0.00789
12	GO:0004765	shikimate kinase activity	5	2	0.15	18	0.00789	0.749	0.00789	0.00789
13	GO:0004301	epoxide hydrolase activity	7	2	0.20	22	0.01595	0.619	0.01595	0.01595
14	GO:0004463	leukotriene-A4 hydrolase activity	7	2	0.20	23	0.01595	0.619	0.01595	1.00000
15	GO:0004764	shikimate 5-dehydrogenase activity	7	2	0.20	24	0.01595	0.340	0.01595	0.01595
16	GO:0016803	ether hydrolase activity	7	2	0.20	25	0.01595	0.619	0.01595	1.00000
17	GO:0016801	hydrolase activity, acting on ether bond...	8	2	0.23	27	0.02087	0.813	0.02087	1.00000
18	GO:0018662	phenol 2-monooxygenase activity	9	2	0.26	28	0.02633	0.837	0.02633	0.02633
19	GO:0019202	amino acid kinase activity	9	2	0.26	29	0.02633	1.000	0.02633	1.00000
20	GO:0003852	2-isopropylmalate synthase activity	1	1	0.03	30	0.02900	1.000	0.02900	1.00000
21	GO:0003856	3-dehydroquinate synthase activity	1	1	0.03	31	0.02900	1.000	0.02900	1.00000
22	GO:0003866	3-phosphoshikimate 1-carboxyvinyltransfe...	1	1	0.03	32	0.02900	1.000	0.02900	0.02900
23	GO:0003876	AMP deaminase activity	1	1	0.03	33	0.02900	0.999	0.02900	0.02900
24	GO:0003937	IMP cyclohydrolase activity	1	1	0.03	34	0.02900	0.999	0.02900	0.02900
25	GO:0003942	N-acetyl-gamma-glutamyl-phosphate reduct...	1	1	0.03	35	0.02900	1.000	0.02900	0.02900
26	GO:0004070	aspartate carbamoyltransferase activity	1	1	0.03	36	0.02900	0.999	0.02900	0.02900
27	GO:0004107	chorismate synthase activity	1	1	0.03	37	0.02900	0.999	0.02900	1.00000
28	GO:0004329	formate-tetrahydrofolate ligase activity	1	1	0.03	38	0.02900	0.999	0.02900	0.02900
29	GO:0004348	glucosylceramidase activity	1	1	0.03	39	0.02900	0.999	0.02900	0.02900
30	GO:0004410	homocitrate synthase activity	1	1	0.03	40	0.02900	0.999	0.02900	1.00000
31	GO:0004413	homoserine kinase activity	1	1	0.03	41	0.02900	1.000	0.02900	0.02900
32	GO:0004475	mannose-1-phosphate guanylyltransferase ...	1	1	0.03	42	0.02900	0.999	0.02900	0.02900
33	GO:0004642	phosphoribosylformylglycinamidine syntha...	1	1	0.03	43	0.02900	0.998	0.02900	0.02900
34	GO:0004643	phosphoribosylaminoimidazolecarboxamide ...	1	1	0.03	44	0.02900	0.999	0.02900	0.02900
35	GO:0004654	polyribonucleotide nucleotidyltransferas...	1	1	0.03	45	0.02900	0.999	0.02900	0.02900
36	GO:0004753	saccharopine dehydrogenase activity	1	1	0.03	46	0.02900	0.998	0.02900	1.00000
37	GO:0004755	saccharopine dehydrogenase (NADP+, L-glu...	1	1	0.03	47	0.02900	0.998	0.02900	0.02900
38	GO:0004795	threonine synthase activity	1	1	0.03	48	0.02900	1.000	0.02900	1.00000
39	GO:0009899	ent-kaurene synthase activity	1	1	0.03	49	0.02900	0.999	0.02900	1.00000
40	GO:0016743	carboxyl- and carbamoyltransferase activ...	1	1	0.03	50	0.02900	0.999	0.02900	1.00000

```
41  GO:0017096 acetylserotonin O-methyltransferase acti...         1           1     0.03              51 0.02900 1.000 0.02900 0.02900
42  GO:0016646 oxidoreductase activity, acting on the C...        11           2     0.32              52 0.03872 0.889 0.03872 1.00000
43  GO:0004497                      monooxygenase activity       241          12     6.99              53 0.04644 0.017 0.04644 0.20655

##########  Cellular component  #############

         GO.ID                                    Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0005618                              cell wall         8           2     0.23               1   0.020 0.87453 0.020  0.020
2   GO:0005737                              cytoplasm       418          18    11.89               2   0.039 0.99367 0.039  0.113

##########  Biological process  #############

         GO.ID                                    Term Annotated Significant Expected Rank in classic classic     KS    elim  weight
1   GO:0006526              arginine biosynthetic process         8           5     0.22              13 8.1e-07 0.9999 8.1e-07 8.1e-07
2   GO:0006418 tRNA aminoacylation for protein translat...        50          11     1.39               9 7.5e-08 0.9995 1.6e-05 7.5e-08
3   GO:0009073 aromatic amino acid family biosynthetic ...        19           5     0.53              19 0.00013 0.1573 0.00013 0.00013
4   GO:0006422               aspartyl-tRNA aminoacylation         7           3     0.19              25 0.00068 0.9995 0.00068 1.00000
5   GO:0006566                threonine metabolic process         3           2     0.08              27 0.00226 1.0000 0.00226 1.00000
6   GO:0019856        pyrimidine base biosynthetic process         5           2     0.14              28 0.00727 0.7321 0.00727 0.00727
7   GO:0006555               methionine metabolic process         8           2     0.22              30 0.01926 0.9951 0.01926 1.00000
8   GO:0016089 aromatic amino acid family biosynthetic ...         8           2     0.22              31 0.01926 0.1447 0.01926 1.00000
9   GO:0009067 aspartate family amino acid biosynthetic...         9           2     0.25              33 0.02431 0.9976 0.02431 1.00000
10  GO:0006807         nitrogen compound metabolic process       262          32     7.29               3 2.7e-13 0.6630 0.02480 0.58629
11  GO:0006074           1,3-beta-glucan metabolic process         1           1     0.03              34 0.02781 0.9999 0.02781 1.00000
12  GO:0006075        1,3-beta-glucan biosynthetic process         1           1     0.03              35 0.02781 0.9999 0.02781 0.02781
13  GO:0007033         vacuole organization and biogenesis         1           1     0.03              36 0.02781 0.9989 0.02781 1.00000
14  GO:0007040        lysosome organization and biogenesis         1           1     0.03              37 0.02781 0.9989 0.02781 0.02781
15  GO:0009272 cell wall biosynthetic process (sensu Fu...         1           1     0.03              38 0.02781 0.9999 0.02781 1.00000
16  GO:0031505 cell wall organization and biogenesis (s...         1           1     0.03              39 0.02781 0.9999 0.02781 1.00000
17  GO:0051273               beta-glucan metabolic process         1           1     0.03              40 0.02781 0.9999 0.02781 1.00000
18  GO:0051274            beta-glucan biosynthetic process         1           1     0.03              41 0.02781 0.9999 0.02781 1.00000
19  GO:0051278 cell wall polysaccharide biosynthetic pr...         1           1     0.03              42 0.02781 0.9999 0.02781 1.00000
20  GO:0019752            carboxylic acid metabolic process       328          34     9.12               5 5.2e-12 0.9756 0.02808 0.53138
21  GO:0006082               organic acid metabolic process       330          34     9.18               6 6.2e-12 0.9759 0.02956 0.73296
22  GO:0008652              amino acid biosynthetic process        96          15     2.67               7 4.0e-08 0.9302 0.03185 1.00000
23  GO:0006575     amino acid derivative metabolic process        26           3     0.72              44 0.03428 0.2572 0.03428 1.00000
24  GO:0009066 aspartate family amino acid metabolic pr...        14           4     0.39              23 0.00046 1.0000 0.03485 0.00046
25  GO:0009309                   amine biosynthetic process        99          15     2.75               8 6.1e-08 0.7664 0.03733 1.00000
26  GO:0000096         sulfur amino acid metabolic process        12           2     0.33              45 0.04222 0.9927 0.04222 1.00000
27  GO:0009082 branched chain family amino acid biosynt...        12           2     0.33              46 0.04222 0.9998 0.04222 0.04222
28  GO:0009698           phenylpropanoid metabolic process        12           2     0.33              47 0.04222 0.3045 0.04222 1.00000
29  GO:0006520                amino acid metabolic process       221          30     6.15               1 1.0e-13 0.9768 0.04480 1.00000
30  GO:0044271      nitrogen compound biosynthetic process       103          15     2.86              12 1.0e-07 0.7374 0.04548 1.00000
```

E.4.2 The 500 most up-regulated genes in *A. niger* CBS 513.88

GO term over-representation results for the 500 most up-regulated and statistically significantly changed genes in *A. niger* CBS 513.88 relative to *A. niger* ATCC 1015. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############
```

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005524	ATP binding	627	69	35.14	6	1.2e-08	0.9360	1.2e-08	1.2e-08
2	GO:0016838	carbon-oxygen lyase activity, acting on ...	5	4	0.28	9	4.6e-05	0.9170	4.6e-05	4.6e-05
3	GO:0004086	carbamoyl-phosphate synthase activity	3	3	0.17	10	0.00017	0.9927	0.00017	0.00017
4	GO:0004812	aminoacyl-tRNA ligase activity	51	19	2.86	1	9.2e-12	0.9986	0.00029	9.2e-12
5	GO:0019202	amino acid kinase activity	9	4	0.50	12	0.00097	1.0000	0.00097	0.00895
6	GO:0016597	amino acid binding	5	3	0.28	13	0.00160	0.9878	0.00160	0.00160
7	GO:0004055	argininosuccinate synthase activity	2	2	0.11	15	0.00313	0.9898	0.00313	0.00313
8	GO:0004813	alanine-tRNA ligase activity	2	2	0.11	16	0.00313	0.9986	0.00313	1.00000
9	GO:0004820	glycine-tRNA ligase activity	2	2	0.11	17	0.00313	0.9963	0.00313	1.00000
10	GO:0046912	transferase activity, transferring acyl ...	13	4	0.73	18	0.00462	0.8864	0.00462	0.00462
11	GO:0004815	aspartate-tRNA ligase activity	8	3	0.45	19	0.00791	0.9986	0.00791	1.00000
12	GO:0003849	3-deoxy-7-phosphoheptulonate synthase ac...	3	2	0.17	20	0.00905	0.9987	0.00905	0.00905
13	GO:0004818	glutamate-tRNA ligase activity	3	2	0.17	21	0.00905	0.9940	0.00905	1.00000
14	GO:0004826	phenylalanine-tRNA ligase activity	3	2	0.17	22	0.00905	0.9999	0.00905	1.00000
15	GO:0004834	tryptophan synthase activity	3	2	0.17	23	0.00905	0.8374	0.00905	0.00905
16	GO:0005338	nucleotide-sugar transporter activity	3	2	0.17	24	0.00905	1.0000	0.00905	0.00905
17	GO:0019904	protein domain specific binding	3	2	0.17	25	0.00905	0.9991	0.00905	0.00905
18	GO:0016744	transferase activity, transferring aldeh...	9	3	0.50	26	0.01138	0.9880	0.01138	0.01138
19	GO:0003984	acetolactate synthase activity	4	2	0.22	27	0.01743	0.7432	0.01743	1.00000
20	GO:0004839	ubiquitin activating enzyme activity	4	2	0.22	28	0.01743	0.9997	0.01743	0.01743
21	GO:0005199	structural constituent of cell wall	4	2	0.22	29	0.01743	0.9812	0.01743	0.01743
22	GO:0008641	small protein activating enzyme activity	4	2	0.22	30	0.01743	0.9997	0.01743	1.00000
23	GO:0016668	oxidoreductase activity, acting on sulfu...	4	2	0.22	31	0.01743	0.8863	0.01743	0.01743
24	GO:0003855	3-dehydroquinate dehydratase activity	5	2	0.28	34	0.02797	0.5738	0.02797	0.02797
25	GO:0004765	shikimate kinase activity	5	2	0.28	35	0.02797	0.7390	0.02797	0.02797
26	GO:0017111	nucleoside-triphosphatase activity	303	25	16.98	36	0.03182	0.8352	0.03182	0.11172
27	GO:0008565	protein transporter activity	80	9	4.48	37	0.03388	0.8548	0.03388	0.03388
28	GO:0003746	translation elongation factor activity	6	2	0.34	38	0.04043	0.9995	0.04043	0.04043
29	GO:0004054	arginine kinase activity	6	2	0.34	39	0.04043	0.9679	0.04043	1.00000
30	GO:0004407	histone deacetylase activity	6	2	0.34	40	0.04043	0.6912	0.04043	0.04043
31	GO:0018110	histone arginine kinase activity	6	2	0.34	41	0.04043	0.9679	0.04043	0.04043
32	GO:0035173	histone kinase activity	6	2	0.34	42	0.04043	0.9679	0.04043	1.00000
33	GO:0000166	nucleotide binding	785	82	44.00	4	3.9e-09	0.9342	0.04667	0.28741
34	GO:0000156	two-component response regulator activit...	15	3	0.84	43	0.04804	0.9215	0.04804	0.04804
35	GO:0008135	translation factor activity, nucleic aci...	36	5	2.02	44	0.04846	0.9290	0.04846	0.57613
36	GO:0045182	translation regulator activity	36	5	2.02	45	0.04846	0.9290	0.04846	1.00000

########## Cellular component #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005643	nuclear pore	15	5	0.85	1	0.0010	0.9656	0.0010	0.0010
2	GO:0009345	glycine-tRNA ligase complex	2	2	0.11	7	0.0032	0.9960	0.0032	0.0032
3	GO:0005737	cytoplasm	418	36	23.60	8	0.0039	0.9848	0.0093	0.0764

########## Biological process #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0006526	arginine biosynthetic process	8	5	0.43	16	2.2e-05	1.00	2.2e-05	2.2e-05
2	GO:0006418	tRNA aminoacylation for protein translat...	50	19	2.72	7	3.2e-12	1.00	0.00022	3.2e-12
3	GO:0009073	aromatic amino acid family biosynthetic ...	19	6	1.03	21	0.00036	0.31	0.00036	1.00000
4	GO:0000059	protein import into nucleus, docking	10	4	0.54	27	0.00138	1.00	0.00138	1.00000

5	GO:0006419	alanyl-tRNA aminoacylation	2	2	0.11	32	0.00294	1.00	0.00294	1.00000
6	GO:0006426	glycyl-tRNA aminoacylation	2	2	0.11	33	0.00294	1.00	0.00294	1.00000
7	GO:0008283	cell proliferation	2	2	0.11	34	0.00294	1.00	0.00294	0.00294
8	GO:0009082	branched chain family amino acid biosynt...	12	4	0.65	35	0.00298	1.00	0.00298	1.00000
9	GO:0006422	aspartyl-tRNA aminoacylation	7	3	0.38	38	0.00471	1.00	0.00471	1.00000
10	GO:0006568	tryptophan metabolic process	8	3	0.43	40	0.00724	0.92	0.00724	0.00724
11	GO:0006424	glutamyl-tRNA aminoacylation	3	2	0.16	47	0.00851	0.99	0.00851	1.00000
12	GO:0006432	phenylalanyl-tRNA aminoacylation	3	2	0.16	48	0.00851	1.00	0.00851	1.00000
13	GO:0006566	threonine metabolic process	3	2	0.16	49	0.00851	1.00	0.00851	1.00000
14	GO:0015780	nucleotide-sugar transport	3	2	0.16	50	0.00851	1.00	0.00851	0.00851
15	GO:0050658	RNA transport	3	2	0.16	51	0.00851	0.97	0.00851	0.00851
16	GO:0019856	pyrimidine base biosynthetic process	5	2	0.27	66	0.02636	0.73	0.02636	0.02636
17	GO:0051169	nuclear transport	16	6	0.87	18	0.00012	1.00	0.03718	1.00000

E.4.3 The 1000 most up-regulated genes in *A. niger* CBS 513.88

GO term over-representation results for the 1000 most up-regulated and statistically significantly changed genes in *A. niger* CBS 513.88 relative to *A. niger* ATCC 1015. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

########## Metabolic function #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005524	ATP binding	627	120	68.17	3	4.3e-11	0.999	4.3e-11	4.3e-11
2	GO:0004812	aminoacyl-tRNA ligase activity	51	21	5.54	6	2.0e-08	0.994	2.0e-08	2.0e-08
3	GO:0016838	carbon-oxygen lyase activity, acting on ...	5	4	0.54	12	0.00063	0.910	0.00063	0.00063
4	GO:0008565	protein transporter activity	80	19	8.70	13	0.00072	0.987	0.00072	0.00072
5	GO:0004086	carbamoyl-phosphate synthase activity	3	3	0.33	16	0.00128	0.974	0.00128	0.00128
6	GO:0008825	cyclopropane-fatty-acyl-phospholipid syn...	3	3	0.33	17	0.00128	1.000	0.00128	0.00128
7	GO:0018110	histone arginine kinase activity	6	4	0.65	19	0.00173	0.981	0.00173	0.00173
8	GO:0005509	calcium ion binding	63	15	6.85	22	0.00248	0.887	0.00248	0.00248
9	GO:0000156	two-component response regulator activit...	15	6	1.63	23	0.00341	0.959	0.00341	0.00341
10	GO:0004839	ubiquitin activating enzyme activity	4	3	0.43	25	0.00470	0.999	0.00470	0.00470
11	GO:0003743	translation initiation factor activity	26	8	2.83	27	0.00491	0.837	0.00491	1.00000
12	GO:0005525	GTP binding	94	19	10.22	28	0.00522	0.997	0.00522	0.00522
13	GO:0016772	transferase activity, transferring phosp...	393	62	42.73	18	0.00129	0.951	0.00527	0.94787
14	GO:0008194	UDP-glycosyltransferase activity	32	9	3.48	30	0.00562	0.380	0.00562	0.01782
15	GO:0016597	amino acid binding	5	3	0.54	32	0.01081	0.958	0.01081	0.01081
16	GO:0043176	amine binding	5	3	0.54	33	0.01081	0.958	0.01081	1.00000
17	GO:0017111	nucleoside-triphosphatase activity	303	46	32.94	34	0.01086	0.977	0.01086	0.03122
18	GO:0016744	transferase activity, transferring aldeh...	9	4	0.98	35	0.01114	0.972	0.01114	0.01114
19	GO:0004055	argininosuccinate synthase activity	2	2	0.22	36	0.01180	0.962	0.01180	0.01180
20	GO:0004748	ribonucleoside-diphosphate reductase act...	2	2	0.22	37	0.01180	0.986	0.01180	0.01180
21	GO:0004813	alanine-tRNA ligase activity	2	2	0.22	38	0.01180	0.995	0.01180	1.00000
22	GO:0004820	glycine-tRNA ligase activity	2	2	0.22	39	0.01180	0.987	0.01180	1.00000
23	GO:0009374	biotin binding	2	2	0.22	40	0.01180	1.000	0.01180	0.01180
24	GO:0016725	oxidoreductase activity, acting on CH2 g...	2	2	0.22	41	0.01180	0.986	0.01180	1.00000
25	GO:0016728	oxidoreductase activity, acting on CH2 g...	2	2	0.22	42	0.01180	0.986	0.01180	1.00000
26	GO:0016462	pyrophosphatase activity	317	47	34.46	43	0.01530	0.939	0.01530	0.60760
27	GO:0016818	hydrolase activity, acting on acid anhyd...	317	47	34.46	44	0.01530	0.939	0.01530	0.76834

28	GO:0016817	hydrolase activity, acting on acid anhyd...	320	47	34.79	45	0.01796	0.920	0.01796	0.67568
29	GO:0004221	ubiquitin thiolesterase activity	21	6	2.28	47	0.02096	0.501	0.02096	0.02096
30	GO:0004843	ubiquitin-specific protease activity	21	6	2.28	48	0.02096	0.501	0.02096	1.00000
31	GO:0019783	small conjugating protein-specific prote...	21	6	2.28	49	0.02096	0.501	0.02096	1.00000
32	GO:0016301	kinase activity	297	46	32.29	31	0.00757	0.976	0.02929	0.94706
33	GO:0035251	UDP-glucosyltransferase activity	17	5	1.85	52	0.03046	0.878	0.03046	1.00000
34	GO:0046527	glucosyltransferase activity	17	5	1.85	53	0.03046	0.878	0.03046	1.00000
35	GO:0019202	amino acid kinase activity	9	6	0.98	10	0.00010	1.000	0.03250	0.03250
36	GO:0003723	RNA binding	76	14	8.26	54	0.03257	0.959	0.03257	0.03257
37	GO:0003849	3-deoxy-7-phosphoheptulonate synthase ac...	3	2	0.33	56	0.03285	0.994	0.03285	0.03285
38	GO:0003978	UDP-glucose 4-epimerase activity	3	2	0.33	57	0.03285	0.888	0.03285	0.03285
39	GO:0004749	ribose phosphate diphosphokinase activit...	3	2	0.33	58	0.03285	0.996	0.03285	0.03285
40	GO:0004818	glutamate-tRNA ligase activity	3	2	0.33	59	0.03285	0.979	0.03285	1.00000
41	GO:0004826	phenylalanine-tRNA ligase activity	3	2	0.33	60	0.03285	1.000	0.03285	1.00000
42	GO:0004834	tryptophan synthase activity	3	2	0.33	61	0.03285	0.828	0.03285	0.03285
43	GO:0005338	nucleotide-sugar transporter activity	3	2	0.33	62	0.03285	1.000	0.03285	0.03285
44	GO:0016979	lipoate-protein ligase activity	3	2	0.33	63	0.03285	0.999	0.03285	0.03285
45	GO:0019904	protein domain specific binding	3	2	0.33	64	0.03285	0.996	0.03285	0.03285
46	GO:0016874	ligase activity	233	51	25.33	9	4.9e-07	0.987	0.03429	0.73766
47	GO:0016779	nucleotidyltransferase activity	77	14	8.37	65	0.03600	0.303	0.03600	0.04993
48	GO:0016758	transferase activity, transferring hexos...	57	11	6.20	66	0.04051	0.139	0.04051	0.70306
49	GO:0046912	transferase activity, transferring acyl ...	13	4	1.41	67	0.04448	0.802	0.04448	0.04448
50	GO:0004815	aspartate-tRNA ligase activity	8	3	0.87	69	0.04716	0.994	0.04716	1.00000
51	GO:0008378	galactosyltransferase activity	8	3	0.87	70	0.04716	0.791	0.04716	1.00000
52	GO:0035250	UDP-galactosyltransferase activity	8	3	0.87	71	0.04716	0.791	0.04716	1.00000

########## Cellular component ##############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005643	nuclear pore	15	8	1.68	2	7.1e-05	0.9967	7.1e-05	7.1e-05
2	GO:0005737	cytoplasm	418	72	46.84	1	2.8e-05	0.9812	0.00036	0.031
3	GO:0044429	mitochondrial part	58	13	6.50	15	0.00983	0.9307	0.00983	1.000
4	GO:0016459	myosin complex	5	3	0.56	18	0.01172	0.9999	0.01172	0.012
5	GO:0009345	glycine-tRNA ligase complex	2	2	0.22	19	0.01252	0.9853	0.01252	0.013
6	GO:0016282	eukaryotic 43S preinitiation complex	2	2	0.22	20	0.01252	0.9993	0.01252	0.013
7	GO:0030133	transport vesicle	6	3	0.67	21	0.02151	0.6615	0.02151	1.000
8	GO:0030658	transport vesicle membrane	6	3	0.67	22	0.02151	0.6615	0.02151	1.000
9	GO:0030660	Golgi-associated vesicle membrane	6	3	0.67	23	0.02151	0.6615	0.02151	1.000
10	GO:0031090	organelle membrane	88	22	9.86	9	0.00016	0.9437	0.02359	1.000
11	GO:0031975	envelope	68	19	7.62	8	9.3e-05	0.8163	0.02492	1.000
12	GO:0031967	organelle envelope	62	18	6.95	7	8.3e-05	0.8353	0.02712	1.000
13	GO:0031966	mitochondrial membrane	40	9	4.48	24	0.02907	0.8072	0.02907	0.029
14	GO:0005740	mitochondrial envelope	47	10	5.27	25	0.03163	0.8126	0.03163	0.504
15	GO:0005798	Golgi-associated vesicle	7	3	0.78	26	0.03456	0.4546	0.03456	1.000
16	GO:0019867	outer membrane	7	3	0.78	27	0.03456	0.9850	0.03456	0.211
17	GO:0044455	mitochondrial membrane part	7	3	0.78	28	0.03456	0.7890	0.03456	1.000
18	GO:0012507	ER to Golgi transport vesicle membrane	3	2	0.34	29	0.03476	0.9568	0.03476	1.000
19	GO:0030127	COPII vesicle coat	3	2	0.34	30	0.03476	0.9568	0.03476	0.035
20	GO:0030134	ER to Golgi transport vesicle	3	2	0.34	31	0.03476	0.9568	0.03476	1.000

########## Biological process ##############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight

1	GO:0006418	tRNA aminoacylation for protein translat...	50	21	5.38	9	1.0e-08	0.994	1.0e-08	1.0e-08
2	GO:0006526	arginine biosynthetic process	8	6	0.86	22	3.5e-05	0.999	3.5e-05	3.5e-05
3	GO:0009082	branched chain family amino acid biosynt...	12	7	1.29	27	7.8e-05	0.999	7.8e-05	1.00000
4	GO:0007049	cell cycle	34	12	3.66	28	0.00013	0.831	0.00013	0.00076
5	GO:0000059	protein import into nucleus, docking	10	6	1.08	31	0.00022	0.999	0.00022	1.00000
6	GO:0009073	aromatic amino acid family biosynthetic ...	19	8	2.04	36	0.00044	0.238	0.00044	1.00000
7	GO:0016043	cell organization and biogenesis	220	43	23.67	24	5.4e-05	0.997	0.00121	1.00000
8	GO:0009067	aspartate family amino acid biosynthetic...	9	5	0.97	49	0.00123	1.000	0.00123	1.00000
9	GO:0050658	RNA transport	3	3	0.32	50	0.00124	0.956	0.00124	0.00124
10	GO:0015031	protein transport	107	26	11.51	23	4.2e-05	0.996	0.00256	0.28175
11	GO:0006092	main pathways of carbohydrate metabolic ...	59	14	6.35	61	0.00318	0.965	0.00318	0.00318
12	GO:0009156	ribonucleoside monophosphate biosyntheti...	16	6	1.72	64	0.00469	0.535	0.00469	1.00000
13	GO:0000160	two-component signal transduction system...	21	7	2.26	66	0.00484	0.963	0.00484	0.00484
14	GO:0006568	tryptophan metabolic process	8	4	0.86	67	0.00650	0.891	0.00650	0.00650
15	GO:0006164	purine nucleotide biosynthetic process	52	12	5.59	74	0.00775	0.655	0.00775	1.00000
16	GO:0000162	tryptophan biosynthetic process	2	2	0.22	77	0.01155	0.999	0.01155	1.00000
17	GO:0006419	alanyl-tRNA aminoacylation	2	2	0.22	78	0.01155	0.994	0.01155	1.00000
18	GO:0006426	glycyl-tRNA aminoacylation	2	2	0.22	79	0.01155	0.987	0.01155	1.00000
19	GO:0008283	cell proliferation	2	2	0.22	80	0.01155	0.989	0.01155	0.01155
20	GO:0009096	aromatic amino acid family biosynthetic ...	2	2	0.22	81	0.01155	0.999	0.01155	1.00000
21	GO:0042435	indole derivative biosynthetic process	2	2	0.22	82	0.01155	0.999	0.01155	1.00000
22	GO:0046219	indolalkylamine biosynthetic process	2	2	0.22	83	0.01155	0.999	0.01155	1.00000
23	GO:0022613	ribonucleoprotein complex biogenesis and...	36	9	3.87	84	0.01186	0.911	0.01186	0.49156
24	GO:0009126	purine nucleoside monophosphate metaboli...	14	5	1.51	85	0.01239	0.459	0.01239	1.00000
25	GO:0009127	purine nucleoside monophosphate biosynth...	14	5	1.51	86	0.01239	0.459	0.01239	1.00000
26	GO:0009167	purine ribonucleoside monophosphate meta...	14	5	1.51	87	0.01239	0.459	0.01239	1.00000
27	GO:0009168	purine ribonucleoside monophosphate bios...	14	5	1.51	88	0.01239	0.459	0.01239	1.00000
28	GO:0006413	translational initiation	25	7	2.69	89	0.01368	0.804	0.01368	0.01368
29	GO:0022618	protein-RNA complex assembly	25	7	2.69	90	0.01368	0.804	0.01368	1.00000
30	GO:0006006	glucose metabolic process	31	8	3.34	91	0.01429	0.985	0.01429	0.01429
31	GO:0046907	intracellular transport	110	24	11.83	39	0.00048	0.989	0.01714	0.41153
32	GO:0051649	establishment of cellular localization	110	24	11.83	40	0.00048	0.989	0.01714	1.00000
33	GO:0007154	cell communication	144	28	15.49	47	0.00120	0.736	0.01876	1.00000
34	GO:0007165	signal transduction	144	28	15.49	48	0.00120	0.736	0.01876	0.18973
35	GO:0051169	nuclear transport	16	9	1.72	16	1.0e-05	0.998	0.01878	1.00000
36	GO:0019318	hexose metabolic process	45	10	4.84	96	0.01884	0.997	0.01884	1.00000
37	GO:0006366	transcription from RNA polymerase II pro...	6	3	0.65	97	0.01930	0.993	0.01930	0.01930
38	GO:0009057	macromolecule catabolic process	79	15	8.50	98	0.01946	0.488	0.01946	0.15368
39	GO:0051641	cellular localization	112	24	12.05	43	0.00064	0.988	0.02073	1.00000
40	GO:0009987	cellular process	3849	445	414.11	21	3.0e-05	0.895	0.02852	0.53055
41	GO:0006913	nucleocytoplasmic transport	17	9	1.83	17	2.0e-05	0.946	0.03030	1.00000
42	GO:0022402	cell cycle process	23	6	2.47	100	0.03085	0.501	0.03085	1.00000
43	GO:0000087	M phase of mitotic cell cycle	7	3	0.75	101	0.03112	0.400	0.03112	0.03112
44	GO:0000278	mitotic cell cycle	7	3	0.75	102	0.03112	0.400	0.03112	1.00000
45	GO:0000279	M phase	7	3	0.75	103	0.03112	0.400	0.03112	1.00000
46	GO:0006422	aspartyl-tRNA aminoacylation	7	3	0.75	104	0.03112	0.995	0.03112	1.00000
47	GO:0022403	cell cycle phase	7	3	0.75	105	0.03112	0.400	0.03112	1.00000
48	GO:0065003	macromolecule complex assembly	66	17	7.10	35	0.00043	0.985	0.03152	0.58041
49	GO:0006424	glutamyl-tRNA aminoacylation	3	2	0.32	106	0.03219	0.979	0.03219	1.00000
50	GO:0006432	phenylalanyl-tRNA aminoacylation	3	2	0.32	107	0.03219	1.000	0.03219	1.00000
51	GO:0006566	threonine metabolic process	3	2	0.32	108	0.03219	1.000	0.03219	0.03219
52	GO:0015780	nucleotide-sugar transport	3	2	0.32	109	0.03219	1.000	0.03219	0.03219
53	GO:0009150	purine ribonucleotide metabolic process	49	10	5.27	111	0.03290	0.611	0.03290	1.00000

54	GO:0009152	purine ribonucleotide biosynthetic proce...	49	10	5.27	112	0.03290	0.611	0.03290	1.00000
55	GO:0043284	biopolymer biosynthetic process	18	5	1.94	113	0.03697	0.790	0.03697	1.00000
56	GO:0046903	secretion	24	6	2.58	114	0.03753	0.999	0.03753	0.04573
57	GO:0006886	intracellular protein transport	82	19	8.82	45	0.00086	0.992	0.03843	1.00000
58	GO:0006520	amino acid metabolic process	221	67	23.78	1	2.2e-16	0.996	0.03844	0.29239
59	GO:0009117	nucleotide metabolic process	85	20	9.15	41	0.00051	0.735	0.03977	1.00000
60	GO:0005996	monosaccharide metabolic process	51	10	5.49	115	0.04216	0.997	0.04216	1.00000
61	GO:0006555	methionine metabolic process	8	3	0.86	117	0.04589	1.000	0.04589	0.04589
62	GO:0044265	cellular macromolecule catabolic process	66	12	7.10	118	0.04645	0.440	0.04645	1.00000
63	GO:0007242	intracellular signaling cascade	74	13	7.96	119	0.04993	0.950	0.04993	0.04993

E.4.4 All genes up-regulated in *A. niger* CBS 513.88

GO term over-representation results for all genes up-regulated and statistically significantly changed in *A. niger* CBS 513.88 relative to *A. niger* ATCC 1015. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

########## Metabolic function #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005524	ATP binding	627	250	160.10	4	3.7e-17	1.00	3.7e-17	3.7e-17
2	GO:0005525	GTP binding	94	49	24.00	9	2.5e-08	0.99	2.5e-08	2.5e-08
3	GO:0004713	protein-tyrosine kinase activity	119	58	30.39	11	3.2e-08	1.00	3.2e-08	5.4e-07
4	GO:0000156	two-component response regulator activit...	15	12	3.83	25	1.5e-05	1.00	1.5e-05	1.5e-05
5	GO:0008565	protein transporter activity	80	44	20.43	8	1.5e-08	0.99	1.9e-05	1.5e-08
6	GO:0003676	nucleic acid binding	1047	331	267.34	15	5.3e-07	0.81	2.4e-05	0.34918
7	GO:0003899	DNA-directed RNA polymerase activity	33	19	8.43	40	8.9e-05	0.88	8.9e-05	1.00000
8	GO:0003743	translation initiation factor activity	26	16	6.64	41	0.00011	0.98	0.00011	1.00000
9	GO:0004004	ATP-dependent RNA helicase activity	42	22	10.72	44	0.00017	0.65	0.00017	0.25345
10	GO:0015462	protein-transporting ATPase activity	42	22	10.72	45	0.00017	0.65	0.00017	1.00000
11	GO:0015616	DNA translocase activity	42	22	10.72	46	0.00017	0.65	0.00017	1.00000
12	GO:0017116	single-stranded DNA-dependent ATP-depend...	42	22	10.72	47	0.00017	0.65	0.00017	0.58384
13	GO:0042624	ATPase activity, uncoupled	42	22	10.72	48	0.00017	0.65	0.00017	0.00017
14	GO:0004812	aminoacyl-tRNA ligase activity	51	25	13.02	52	0.00025	0.97	0.00025	0.00025
15	GO:0004221	ubiquitin thiolesterase activity	21	13	5.36	57	0.00045	0.91	0.00045	0.00045
16	GO:0005515	protein binding	125	49	31.92	61	0.00048	0.85	0.00048	1.00000
17	GO:0008605	protein kinase CK2 regulator activity	34	18	8.68	63	0.00056	0.87	0.00056	0.00056
18	GO:0042625	ATPase activity, coupled to transmembran...	97	44	24.77	26	1.6e-05	0.92	0.00058	2.1e-05
19	GO:0016838	carbon-oxygen lyase activity, acting on ...	5	5	1.28	69	0.00108	0.99	0.00108	0.00108
20	GO:0004682	protein kinase CK2 activity	33	17	8.43	70	0.00119	0.70	0.00119	1.00000
21	GO:0004691	cAMP-dependent protein kinase activity	33	17	8.43	71	0.00119	0.70	0.00119	1.00000
22	GO:0003774	motor activity	23	13	5.87	72	0.00150	0.98	0.00150	0.00150
23	GO:0005083	small GTPase regulator activity	7	6	1.79	73	0.00150	1.00	0.00150	0.00150
24	GO:0017111	nucleoside-triphosphatase activity	303	115	77.37	16	6.5e-07	0.98	0.00154	0.00284
25	GO:0016758	transferase activity, transferring hexos...	57	29	14.55	32	3.3e-05	0.87	0.00205	0.00392
26	GO:0008603	cAMP-dependent protein kinase regulator ...	35	17	8.94	75	0.00271	0.68	0.00271	0.00271
27	GO:0004707	MAP kinase activity	27	14	6.89	76	0.00297	0.62	0.00297	0.10809
28	GO:0004674	protein serine/threonine kinase activity	153	67	39.07	14	5.0e-07	1.00	0.00332	2.7e-05
29	GO:0035251	UDP-glucosyltransferase activity	17	10	4.34	79	0.00362	0.97	0.00362	1.00000
30	GO:0016307	phosphatidylinositol phosphate kinase ac...	25	13	6.38	81	0.00403	0.79	0.00403	1.00000

31	GO:0035004	phosphoinositide 3-kinase activity	25	13	6.38	82	0.00403	0.57	0.00403	1.00000
32	GO:0000155	two-component sensor activity	15	9	3.83	83	0.00483	0.99	0.00483	0.00483
33	GO:0004308	exo-alpha-sialidase activity	31	15	7.92	86	0.00498	0.12	0.00498	0.00498
34	GO:0004721	phosphoprotein phosphatase activity	31	15	7.92	87	0.00498	0.98	0.00498	0.00745
35	GO:0018110	histone arginine kinase activity	6	5	1.53	89	0.00510	0.91	0.00510	0.00510
36	GO:0019200	carbohydrate kinase activity	34	16	8.68	92	0.00531	0.80	0.00531	0.00531
37	GO:0004693	cyclin-dependent protein kinase activity	23	12	5.87	94	0.00550	0.73	0.00550	1.00000
38	GO:0008047	enzyme activator activity	26	13	6.64	95	0.00621	0.69	0.00621	1.00000
39	GO:0015662	ATPase activity, coupled to transmembran...	26	13	6.64	96	0.00621	0.99	0.00621	1.00000
40	GO:0004339	glucan 1,4-alpha-glucosidase activity	32	15	8.17	97	0.00720	0.78	0.00720	0.00720
41	GO:0016779	nucleotidyltransferase activity	77	38	19.66	22	5.2e-06	0.76	0.00725	2.0e-05
42	GO:0003684	damaged DNA binding	16	9	4.09	98	0.00857	0.92	0.00857	0.00857
43	GO:0016879	ligase activity, forming carbon-nitrogen...	121	43	30.90	99	0.00869	0.78	0.00869	0.00555
44	GO:0019207	kinase regulator activity	58	29	14.81	35	5.0e-05	0.69	0.01106	1.00000
45	GO:0019887	protein kinase regulator activity	58	29	14.81	36	5.0e-05	0.69	0.01106	1.00000
46	GO:0004680	casein kinase activity	55	28	14.04	33	4.4e-05	0.55	0.01108	0.44190
47	GO:0004690	cyclic nucleotide-dependent protein kina...	55	28	14.04	34	4.4e-05	0.55	0.01108	0.44190
48	GO:0001565	phorbol ester receptor activity	22	11	5.62	102	0.01161	0.64	0.01161	1.00000
49	GO:0004675	transmembrane receptor protein serine/th...	22	11	5.62	103	0.01161	0.64	0.01161	0.01161
50	GO:0004676	3-phosphoinositide-dependent protein kin...	22	11	5.62	104	0.01161	0.64	0.01161	1.00000
51	GO:0004677	DNA-dependent protein kinase activity	22	11	5.62	105	0.01161	0.64	0.01161	1.00000
52	GO:0004679	AMP-activated protein kinase activity	22	11	5.62	106	0.01161	0.64	0.01161	1.00000
53	GO:0004681	casein kinase I activity	22	11	5.62	107	0.01161	0.64	0.01161	1.00000
54	GO:0004686	eukaryotic elongation factor-2 kinase ac...	22	11	5.62	108	0.01161	0.64	0.01161	0.01161
55	GO:0004688	multifunctional calcium- and calmodulin-...	22	11	5.62	109	0.01161	0.64	0.01161	0.01161
56	GO:0004689	phosphorylase kinase activity	22	11	5.62	110	0.01161	0.64	0.01161	0.01161
57	GO:0004692	cGMP-dependent protein kinase activity	22	11	5.62	111	0.01161	0.64	0.01161	1.00000
58	GO:0004694	eukaryotic translation initiation factor...	22	11	5.62	112	0.01161	0.64	0.01161	1.00000
59	GO:0004695	galactosyltransferase-associated kinase ...	22	11	5.62	113	0.01161	0.64	0.01161	1.00000
60	GO:0004696	glycogen synthase kinase 3 activity	22	11	5.62	114	0.01161	0.64	0.01161	1.00000
61	GO:0004697	protein kinase C activity	22	11	5.62	115	0.01161	0.64	0.01161	1.00000
62	GO:0004698	calcium-dependent protein kinase C activ...	22	11	5.62	116	0.01161	0.64	0.01161	0.01161
63	GO:0004700	atypical protein kinase C activity	22	11	5.62	117	0.01161	0.64	0.01161	0.01161
64	GO:0004701	diacylglycerol-activated phospholipid-de...	22	11	5.62	118	0.01161	0.64	0.01161	0.01161
65	GO:0004703	G-protein coupled receptor kinase activi...	22	11	5.62	119	0.01161	0.64	0.01161	1.00000
66	GO:0004704	NF-kappaB-inducing kinase activity	22	11	5.62	120	0.01161	0.64	0.01161	0.01161
67	GO:0004705	JUN kinase activity	22	11	5.62	121	0.01161	0.64	0.01161	0.01161
68	GO:0004706	JUN kinase kinase kinase activity	22	11	5.62	122	0.01161	0.64	0.01161	0.01161
69	GO:0004708	MAP kinase kinase activity	22	11	5.62	123	0.01161	0.64	0.01161	0.44421
70	GO:0004709	MAP kinase kinase kinase activity	22	11	5.62	124	0.01161	0.64	0.01161	1.00000
71	GO:0004710	MAP/ERK kinase kinase activity	22	11	5.62	125	0.01161	0.64	0.01161	0.01161
72	GO:0004711	ribosomal protein S6 kinase activity	22	11	5.62	126	0.01161	0.64	0.01161	1.00000
73	GO:0004712	protein threonine/tyrosine kinase activi...	22	11	5.62	127	0.01161	0.64	0.01161	1.00000
74	GO:0004714	transmembrane receptor protein tyrosine ...	22	11	5.62	128	0.01161	0.64	0.01161	1.00000
75	GO:0004715	non-membrane spanning protein tyrosine k...	22	11	5.62	129	0.01161	0.64	0.01161	1.00000
76	GO:0004716	receptor signaling protein tyrosine kina...	22	11	5.62	130	0.01161	0.64	0.01161	1.00000
77	GO:0004718	Janus kinase activity	22	11	5.62	131	0.01161	0.64	0.01161	0.01161
78	GO:0008338	MAP kinase 1 activity	22	11	5.62	132	0.01161	0.64	0.01161	0.01161
79	GO:0008339	MP kinase activity	22	11	5.62	133	0.01161	0.64	0.01161	0.01161
80	GO:0008349	MAP kinase kinase kinase kinase activity	22	11	5.62	134	0.01161	0.64	0.01161	0.01161
81	GO:0008384	IkappaB kinase activity	22	11	5.62	135	0.01161	0.64	0.01161	1.00000
82	GO:0008545	JUN kinase kinase activity	22	11	5.62	136	0.01161	0.64	0.01161	0.01161
83	GO:0008607	phosphorylase kinase regulator activity	22	11	5.62	137	0.01161	0.64	0.01161	0.01161

84	GO:0008819	cobinamide kinase activity	22	11	5.62	138	0.01161	0.64	0.01161	0.01161
85	GO:0016538	cyclin-dependent protein kinase regulato...	22	11	5.62	139	0.01161	0.64	0.01161	0.01161
86	GO:0016908	MAP kinase 2 activity	22	11	5.62	140	0.01161	0.64	0.01161	0.01161
87	GO:0016909	SAP kinase activity	22	11	5.62	141	0.01161	0.64	0.01161	1.00000
88	GO:0018720	phenol kinase activity	22	11	5.62	142	0.01161	0.64	0.01161	0.01161
89	GO:0019199	transmembrane receptor protein kinase ac...	22	11	5.62	143	0.01161	0.64	0.01161	1.00000
90	GO:0019209	kinase activator activity	22	11	5.62	144	0.01161	0.64	0.01161	1.00000
91	GO:0019912	cyclin-dependent protein kinase activati...	22	11	5.62	145	0.01161	0.64	0.01161	0.01161
92	GO:0019914	cyclin-dependent protein kinase activati...	22	11	5.62	146	0.01161	0.64	0.01161	0.01161
93	GO:0030295	protein kinase activator activity	22	11	5.62	147	0.01161	0.64	0.01161	1.00000
94	GO:0042556	eukaryotic elongation factor-2 kinase re...	22	11	5.62	148	0.01161	0.64	0.01161	0.44421
95	GO:0042557	eukaryotic elongation factor-2 kinase ac...	22	11	5.62	149	0.01161	0.64	0.01161	0.01161
96	GO:0003682	chromatin binding	7	5	1.79	151	0.01410	0.81	0.01410	1.00000
97	GO:0004576	oligosaccharyl transferase activity	12	7	3.06	152	0.01595	0.87	0.01595	1.00000
98	GO:0003849	3-deoxy-7-phosphoheptulonate synthase ac...	3	3	0.77	153	0.01662	0.97	0.01662	0.01662
99	GO:0003978	UDP-glucose 4-epimerase activity	3	3	0.77	154	0.01662	0.99	0.01662	0.01662
100	GO:0004086	carbamoyl-phosphate synthase activity	3	3	0.77	155	0.01662	0.87	0.01662	1.00000
101	GO:0004749	ribose phosphate diphosphokinase activit...	3	3	0.77	156	0.01662	1.00	0.01662	1.00000
102	GO:0004805	trehalose-phosphatase activity	3	3	0.77	157	0.01662	0.99	0.01662	0.01662
103	GO:0005338	nucleotide-sugar transporter activity	3	3	0.77	158	0.01662	1.00	0.01662	0.01662
104	GO:0008825	cyclopropane-fatty-acyl-phospholipid syn...	3	3	0.77	159	0.01662	1.00	0.01662	0.01662
105	GO:0016979	lipoate-protein ligase activity	3	3	0.77	160	0.01662	1.00	0.01662	1.00000
106	GO:0019203	carbohydrate phosphatase activity	3	3	0.77	161	0.01662	0.99	0.01662	1.00000
107	GO:0016597	amino acid binding	5	4	1.28	162	0.01687	0.95	0.01687	0.01687
108	GO:0043176	amine binding	5	4	1.28	163	0.01687	0.95	0.01687	1.00000
109	GO:0008443	phosphofructokinase activity	23	11	5.87	164	0.01722	0.62	0.01722	1.00000
110	GO:0005509	calcium ion binding	63	24	16.09	165	0.01840	0.96	0.01840	0.01840
111	GO:0004683	calmodulin regulated protein kinase acti...	29	13	7.40	166	0.01854	0.69	0.01854	1.00000
112	GO:0004725	protein tyrosine phosphatase activity	10	6	2.55	169	0.02179	0.99	0.02179	1.00000
113	GO:0004175	endopeptidase activity	159	52	40.60	170	0.02419	0.69	0.02419	0.03375
114	GO:0004872	receptor activity	55	21	14.04	171	0.02573	0.20	0.02573	1.00000
115	GO:0008237	metallopeptidase activity	88	31	22.47	172	0.02668	0.55	0.02668	0.20938
116	GO:0004888	transmembrane receptor activity	52	20	13.28	173	0.02684	0.23	0.02684	0.90419
117	GO:0046912	transferase activity, transferring acyl ...	13	7	3.32	174	0.02705	0.88	0.02705	0.02705
118	GO:0000030	mannosyltransferase activity	16	8	4.09	176	0.03045	0.99	0.03045	1.00000
119	GO:0008375	acetylglucosaminyltransferase activity	16	8	4.09	177	0.03045	0.53	0.03045	1.00000
120	GO:0003723	RNA binding	76	27	19.41	178	0.03321	0.91	0.03321	1.00000
121	GO:0008483	transaminase activity	28	12	7.15	179	0.03400	0.81	0.03400	0.03400
122	GO:0016740	transferase activity	876	303	223.68	7	4.6e-11	0.99	0.03572	0.99977
123	GO:0004197	cysteine-type endopeptidase activity	57	21	14.55	180	0.03830	0.93	0.03830	0.29875
124	GO:0016791	phosphoric monoester hydrolase activity	69	30	17.62	68	0.00084	0.96	0.03926	0.76400
125	GO:0003746	translation elongation factor activity	6	4	1.53	181	0.04040	0.99	0.04040	1.00000
126	GO:0003825	alpha,alpha-trehalose-phosphate synthase...	6	4	1.53	182	0.04040	0.99	0.04040	1.00000
127	GO:0004100	chitin synthase activity	6	4	1.53	183	0.04040	0.73	0.04040	1.00000
128	GO:0004437	inositol or phosphatidylinositol phospha...	14	7	3.57	184	0.04241	0.73	0.04241	0.30027
129	GO:0016887	ATPase activity	225	85	57.45	28	2.4e-05	0.97	0.04690	1.00000

########## Cellular component #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005737	cytoplasm	418	165	115.31	3	3.5e-09	0.938	1.3e-07	0.28367
2	GO:0005643	nuclear pore	15	13	4.14	6	2.9e-06	0.989	2.9e-06	2.9e-06
3	GO:0005622	intracellular	1314	438	362.48	1	6.0e-13	0.872	0.00019	8.3e-09

4	GO:0030120	vesicle coat	15	11	4.14	14	0.00029	0.982	0.00029	0.00029
5	GO:0044424	intracellular part	1244	410	343.17	2	2.6e-10	0.446	0.00084	1.00000
6	GO:0005956	protein kinase CK2 complex	34	18	9.38	29	0.00144	0.778	0.00144	1.00000
7	GO:0016459	myosin complex	5	5	1.38	30	0.00158	1.000	0.00158	0.00158
8	GO:0019867	outer membrane	7	6	1.93	31	0.00232	0.998	0.00232	0.07539
9	GO:0044444	cytoplasmic part	305	110	84.14	26	0.00032	0.922	0.00362	1.00000
10	GO:0005952	cAMP-dependent protein kinase complex	35	17	9.66	37	0.00624	0.565	0.00624	1.00000
11	GO:0030658	transport vesicle membrane	6	5	1.66	38	0.00731	0.793	0.00731	1.00000
12	GO:0030660	Golgi-associated vesicle membrane	6	5	1.66	39	0.00731	0.793	0.00731	1.00000
13	GO:0030118	clathrin coat	11	7	3.03	41	0.01323	0.996	0.01323	1.00000
14	GO:0030125	clathrin vesicle coat	11	7	3.03	42	0.01323	0.996	0.01323	1.00000
15	GO:0030136	clathrin-coated vesicle	11	7	3.03	43	0.01323	0.996	0.01323	1.00000
16	GO:0030665	clathrin coated vesicle membrane	11	7	3.03	44	0.01323	0.996	0.01323	1.00000
17	GO:0043234	protein complex	475	166	131.03	13	4.7e-05	0.891	0.01587	0.05045
18	GO:0012507	ER to Golgi transport vesicle membrane	3	3	0.83	49	0.02092	0.819	0.02092	1.00000
19	GO:0030127	COPII vesicle coat	3	3	0.83	50	0.02092	0.819	0.02092	1.00000
20	GO:0030134	ER to Golgi transport vesicle	3	3	0.83	51	0.02092	0.819	0.02092	1.00000
21	GO:0005741	mitochondrial outer membrane	5	4	1.38	52	0.02244	0.999	0.02244	0.02244
22	GO:0031968	organelle outer membrane	5	4	1.38	53	0.02244	0.999	0.02244	1.00000
23	GO:0005739	mitochondrion	71	27	19.59	56	0.03388	0.957	0.03388	1.00000
24	GO:0005886	plasma membrane	8	5	2.21	57	0.04091	0.935	0.04091	1.00000
25	GO:0044459	plasma membrane part	8	5	2.21	58	0.04091	0.935	0.04091	1.00000

########## Biological process #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0044267	cellular protein metabolic process	926	316	228.61	3	2.7e-13	1.00	3.7e-05	0.13598
2	GO:0000160	two-component signal transduction system...	21	14	5.18	43	5.6e-05	1.00	5.6e-05	1.00000
3	GO:0007242	intracellular signaling cascade	74	38	18.27	24	5.8e-07	0.99	8.3e-05	1.00000
4	GO:0006418	tRNA aminoacylation for protein translat...	50	25	12.34	44	9.0e-05	0.97	9.0e-05	0.56831
5	GO:0007049	cell cycle	34	19	8.39	47	9.3e-05	0.95	9.3e-05	0.00011
6	GO:0015031	protein transport	107	55	26.42	10	1.6e-09	0.99	0.00014	2.1e-06
7	GO:0006886	intracellular protein transport	82	40	20.24	27	1.7e-06	0.99	0.00016	1.00000
8	GO:0006413	translational initiation	25	15	6.17	54	0.00018	0.98	0.00018	1.00000
9	GO:0006468	protein amino acid phosphorylation	198	71	48.88	56	0.00022	0.93	0.00022	1.00000
10	GO:0006526	arginine biosynthetic process	8	7	1.97	61	0.00035	0.99	0.00035	0.00035
11	GO:0000059	protein import into nucleus, docking	10	8	2.47	63	0.00037	1.00	0.00037	1.00000
12	GO:0006099	tricarboxylic acid cycle	15	10	3.70	67	0.00070	1.00	0.00070	0.24567
13	GO:0006261	DNA-dependent DNA replication	23	13	5.68	73	0.00106	0.97	0.00106	0.03166
14	GO:0006913	nucleocytoplasmic transport	17	14	4.20	25	9.2e-07	0.99	0.00120	1.00000
15	GO:0009067	aspartate family amino acid biosynthetic...	9	7	2.22	76	0.00122	1.00	0.00122	0.00122
16	GO:0007264	small GTPase mediated signal transductio...	40	19	9.87	77	0.00139	0.91	0.00139	1.00000
17	GO:0006486	protein amino acid glycosylation	16	10	3.95	78	0.00145	1.00	0.00145	1.00000
18	GO:0043283	biopolymer metabolic process	1100	344	271.56	17	7.5e-09	1.00	0.00150	0.63077
19	GO:0016051	carbohydrate biosynthetic process	24	13	5.92	82	0.00180	1.00	0.00180	1.00000
20	GO:0006796	phosphate metabolic process	265	98	65.42	29	3.0e-06	0.99	0.00239	0.24785
21	GO:0009082	branched chain family amino acid biosynt...	12	8	2.96	83	0.00252	1.00	0.00252	0.00252
22	GO:0046907	intracellular transport	110	55	27.16	15	5.9e-09	0.99	0.00379	0.00086
23	GO:0006555	methionine metabolic process	8	6	1.97	92	0.00392	1.00	0.00392	0.00392
24	GO:0051169	nuclear transport	16	13	3.95	31	3.1e-06	0.99	0.00425	1.00000
25	GO:0006996	organelle organization and biogenesis	96	39	23.70	62	0.00037	0.92	0.00477	0.96480
26	GO:0044238	primary metabolic process	2361	705	582.87	1	4.5e-17	0.99	0.00641	0.97453
27	GO:0009156	ribonucleoside monophosphate biosyntheti...	16	9	3.95	93	0.00675	0.51	0.00675	1.00000

28	GO:0042254	ribosome biogenesis and assembly	11	7	2.72	95	0.00696	0.97	0.00696	0.00696
29	GO:0019318	hexose metabolic process	45	19	11.11	96	0.00712	0.99	0.00712	0.67548
30	GO:0009073	aromatic amino acid family biosynthetic ...	19	10	4.69	97	0.00799	0.50	0.00799	0.03697
31	GO:0009152	purine ribonucleotide biosynthetic proce...	49	20	12.10	99	0.00908	0.57	0.00908	1.00000
32	GO:0015980	energy derivation by oxidation of organi...	68	31	16.79	50	0.00013	0.97	0.01050	1.00000
33	GO:0022406	membrane docking	7	5	1.73	101	0.01211	0.94	0.01211	1.00000
34	GO:0048278	vesicle docking	7	5	1.73	102	0.01211	0.94	0.01211	0.01211
35	GO:0016192	vesicle-mediated transport	23	11	5.68	103	0.01330	1.00	0.01330	0.89520
36	GO:0006606	protein import into nucleus	15	12	3.70	36	1.0e-05	0.99	0.01459	1.0e-05
37	GO:0051170	nuclear import	15	12	3.70	37	1.0e-05	0.99	0.01459	1.00000
38	GO:0006163	purine nucleotide metabolic process	52	23	12.84	80	0.00153	0.61	0.01470	0.01470
39	GO:0006164	purine nucleotide biosynthetic process	52	23	12.84	81	0.00153	0.61	0.01470	1.00000
40	GO:0006188	IMP biosynthetic process	5	4	1.23	105	0.01486	0.72	0.01486	1.00000
41	GO:0006189	'de novo' IMP biosynthetic process	5	4	1.23	106	0.01486	0.72	0.01486	0.01486
42	GO:0009086	methionine biosynthetic process	5	4	1.23	107	0.01486	1.00	0.01486	1.00000
43	GO:0046040	IMP metabolic process	5	4	1.23	108	0.01486	0.72	0.01486	1.00000
44	GO:0006403	RNA localization	3	3	0.74	109	0.01502	0.79	0.01502	1.00000
45	GO:0006566	threonine metabolic process	3	3	0.74	110	0.01502	1.00	0.01502	0.01502
46	GO:0015780	nucleotide-sugar transport	3	3	0.74	111	0.01502	1.00	0.01502	0.01502
47	GO:0050657	nucleic acid transport	3	3	0.74	112	0.01502	0.79	0.01502	1.00000
48	GO:0050658	RNA transport	3	3	0.74	113	0.01502	0.79	0.01502	0.01502
49	GO:0051236	establishment of RNA localization	3	3	0.74	114	0.01502	0.79	0.01502	1.00000
50	GO:0006464	protein modification	368	130	90.85	26	1.3e-06	1.00	0.01580	1.00000
51	GO:0009987	cellular process	3849	1021	950.22	7	1.8e-11	0.91	0.01619	0.86599
52	GO:0051276	chromosome organization and biogenesis	42	17	10.37	115	0.01705	0.81	0.01705	0.10440
53	GO:0006470	protein amino acid dephosphorylation	18	9	4.44	116	0.01764	0.99	0.01764	1.00000
54	GO:0016311	dephosphorylation	18	9	4.44	117	0.01764	0.99	0.01764	1.00000
55	GO:0043284	biopolymer biosynthetic process	18	9	4.44	118	0.01764	0.97	0.01764	1.00000
56	GO:0006508	proteolysis	271	82	66.90	119	0.01850	0.23	0.01850	1.00000
57	GO:0007166	cell surface receptor linked signal tran...	30	13	7.41	120	0.01916	0.45	0.01916	1.00000
58	GO:0007186	G-protein coupled receptor protein signa...	30	13	7.41	121	0.01916	0.45	0.01916	0.03503
59	GO:0007017	microtubule-based process	24	11	5.92	122	0.01919	0.80	0.01919	0.01919
60	GO:0046903	secretion	24	11	5.92	123	0.01919	1.00	0.01919	0.00800
61	GO:0009057	macromolecule catabolic process	79	28	19.50	124	0.02041	0.55	0.02041	0.75479
62	GO:0044265	cellular macromolecule catabolic process	66	24	16.29	125	0.02219	0.61	0.02219	1.00000
63	GO:0016070	RNA metabolic process	543	164	134.05	74	0.00109	0.95	0.02310	0.11112
64	GO:0006006	glucose metabolic process	31	13	7.65	126	0.02573	0.98	0.02573	0.02573
65	GO:0006544	glycine metabolic process	8	5	1.97	127	0.02577	0.99	0.02577	0.02577
66	GO:0006568	tryptophan metabolic process	8	5	1.97	128	0.02577	0.87	0.02577	0.02577
67	GO:0006586	indolalkylamine metabolic process	8	5	1.97	129	0.02577	0.87	0.02577	1.00000
68	GO:0006887	exocytosis	8	5	1.97	130	0.02577	0.96	0.02577	1.00000
69	GO:0042430	indole and derivative metabolic process	8	5	1.97	131	0.02577	0.87	0.02577	1.00000
70	GO:0042434	indole derivative metabolic process	8	5	1.97	132	0.02577	0.87	0.02577	1.00000
71	GO:0006092	main pathways of carbohydrate metabolic ...	59	27	14.57	59	0.00031	0.96	0.02631	0.00059
72	GO:0007018	microtubule-based movement	19	9	4.69	133	0.02632	0.50	0.02632	0.43160
73	GO:0030705	cytoskeleton-dependent intracellular tra...	19	9	4.69	134	0.02632	0.50	0.02632	1.00000
74	GO:0045045	secretory pathway	22	10	5.43	135	0.02684	1.00	0.02684	0.43152
75	GO:0008219	cell death	11	6	2.72	139	0.03219	0.88	0.03219	1.00000
76	GO:0016265	death	11	6	2.72	140	0.03219	0.88	0.03219	1.00000
77	GO:0016310	phosphorylation	247	89	60.98	41	2.9e-05	0.99	0.03306	7.4e-05
78	GO:0007010	cytoskeleton organization and biogenesis	32	13	7.90	141	0.03382	0.92	0.03382	0.67653
79	GO:0009165	nucleotide biosynthetic process	68	30	16.79	60	0.00033	0.79	0.03554	0.02154
80	GO:0009126	purine nucleoside monophosphate metaboli...	14	7	3.46	142	0.03565	0.44	0.03565	1.00000

81	GO:0009127	purine nucleoside monophosphate biosynth...	14	7	3.46	143	0.03565	0.44	0.03565	1.00000
82	GO:0009167	purine ribonucleoside monophosphate meta...	14	7	3.46	144	0.03565	0.44	0.03565	1.00000
83	GO:0009168	purine ribonucleoside monophosphate bios...	14	7	3.46	145	0.03565	0.44	0.03565	1.00000
84	GO:0005992	trehalose biosynthetic process	6	4	1.48	146	0.03588	0.99	0.03588	0.03588
85	GO:0006366	transcription from RNA polymerase II pro...	6	4	1.48	147	0.03588	0.98	0.03588	0.03588
86	GO:0006888	ER to Golgi vesicle-mediated transport	6	4	1.48	148	0.03588	0.93	0.03588	1.00000
87	GO:0006904	vesicle docking during exocytosis	6	4	1.48	149	0.03588	0.91	0.03588	1.00000
88	GO:0046351	disaccharide biosynthetic process	6	4	1.48	150	0.03588	0.99	0.03588	1.00000
89	GO:0022402	cell cycle process	23	10	5.68	151	0.03725	0.92	0.03725	1.00000
90	GO:0050794	regulation of cellular process	437	123	107.88	152	0.04554	0.82	0.04554	0.33430
91	GO:0046164	alcohol catabolic process	30	12	7.41	153	0.04589	0.97	0.04589	1.00000
92	GO:0006012	galactose metabolic process	9	5	2.22	154	0.04637	0.97	0.04637	0.04637
93	GO:0006414	translational elongation	9	5	2.22	155	0.04637	0.99	0.04637	1.00000
94	GO:0006551	leucine metabolic process	4	3	0.99	156	0.04897	0.98	0.04897	1.00000
95	GO:0009098	leucine biosynthetic process	4	3	0.99	157	0.04897	0.98	0.04897	1.00000
96	GO:0009225	nucleotide-sugar metabolic process	4	3	0.99	158	0.04897	0.98	0.04897	0.04897

E.4.5 The 250 most up-regulated genes in *A. niger* ATCC 1015

GO term over-representation results for the 250 most up-regulated and statistically significantly changed genes in *A. niger* ATCC 1015 relative to *A. niger* CBS 513.88. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

########## Metabolic function #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0016491	oxidoreductase activity	1146	44	22.43	1	1.6e-06	0.01354	5.3e-05	0.0078
2	GO:0003824	catalytic activity	3853	95	75.41	2	1.2e-05	7.4e-08	0.0029	0.2071
3	GO:0016616	oxidoreductase activity, acting on the C...	188	10	3.68	4	0.00355	0.00199	0.0036	1.0000
4	GO:0000252	C-3 sterol dehydrogenase (C-4 sterol dec...	10	2	0.20	5	0.01542	0.13522	0.0154	0.0154
5	GO:0000253	3-keto sterol reductase activity	10	2	0.20	6	0.01542	0.13522	0.0154	0.0154
6	GO:0004495	mevaldate reductase activity	10	2	0.20	7	0.01542	0.13522	0.0154	0.0154
7	GO:0018451	epoxide dehydrogenase activity	10	2	0.20	8	0.01542	0.13522	0.0154	0.0154
8	GO:0018452	5-exo-hydroxycamphor dehydrogenase activ...	10	2	0.20	9	0.01542	0.13522	0.0154	0.0154
9	GO:0018453	2-hydroxytetrahydrofuran dehydrogenase a...	10	2	0.20	10	0.01542	0.13522	0.0154	0.0154
10	GO:0048258	3-ketoglucose-reductase activity	10	2	0.20	11	0.01542	0.13522	0.0154	0.0154
11	GO:0016207	4-coumarate-CoA ligase activity	11	2	0.22	12	0.01861	0.13742	0.0186	0.0186
12	GO:0004645	phosphorylase activity	1	1	0.02	13	0.01957	0.99968	0.0196	1.0000
13	GO:0008184	glycogen phosphorylase activity	1	1	0.02	14	0.01957	0.99968	0.0196	0.0196
14	GO:0008732	L-allo-threonine aldolase activity	1	1	0.02	15	0.01957	0.99976	0.0196	0.0196
15	GO:0008941	nitric oxide dioxygenase activity	1	1	0.02	16	0.01957	0.99973	0.0196	0.0196
16	GO:0015109	chromate transporter activity	1	1	0.02	17	0.01957	0.99929	0.0196	0.0196
17	GO:0018802	2,4-dihydroxyhept-2-ene-1,7-dioate aldol...	1	1	0.02	18	0.01957	0.99976	0.0196	0.0196
18	GO:0003939	L-iditol 2-dehydrogenase activity	12	2	0.23	19	0.02205	0.84558	0.0220	0.0220
19	GO:0004090	carbonyl reductase (NADPH) activity	12	2	0.23	20	0.02205	0.14550	0.0220	0.0220
20	GO:0008875	gluconate dehydrogenase activity	13	2	0.25	21	0.02573	0.18496	0.0257	0.0257
21	GO:0046873	metal ion transporter activity	34	3	0.67	22	0.02812	0.78788	0.0281	0.1144
22	GO:0016863	intramolecular oxidoreductase activity, ...	14	2	0.27	23	0.02963	0.47077	0.0296	0.0296
23	GO:0004448	isocitrate dehydrogenase activity	16	2	0.31	24	0.03810	0.21863	0.0381	0.0381
24	GO:0016405	CoA-ligase activity	16	2	0.31	25	0.03810	0.06892	0.0381	1.0000

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25  GO:0016878                  acid-thiol ligase activity        16           2     0.31              26 0.03810 0.06892  0.0381 1.0000
26  GO:0004470                       malic enzyme activity         2           1     0.04              27 0.03877 1.00000  0.0388 0.0388
27  GO:0008398              sterol 14-demethylase activity         2           1     0.04              28 0.03877 0.98407  0.0388 0.0388
28  GO:0032451                        demethylase activity         2           1     0.04              29 0.03877 0.98407  0.0388 1.0000
29  GO:0004023 alcohol dehydrogenase activity, metal io...        17           2     0.33              30 0.04264 0.76231  0.0426 0.0426
30  GO:0004024 alcohol dehydrogenase activity, zinc-dep...        17           2     0.33              31 0.04264 0.76231  0.0426 0.0426
31  GO:0004025 alcohol dehydrogenase activity, iron-dep...        17           2     0.33              32 0.04264 0.76231  0.0426 0.0426
32  GO:0004022              alcohol dehydrogenase activity        18           2     0.35              33 0.04737 0.76708  0.0474 1.0000

##########  Cellular component  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1   GO:0005576                    extracellular region        25           2     0.30               1   0.036  0.9268 0.036  0.036
2   GO:0030288    periplasmic space (sensu ProteoBacteria)         4           1     0.05               2   0.047  0.9996 0.047  0.047
3   GO:0042597                         periplasmic space         4           1     0.05               3   0.047  0.9996 0.047  1.000

##########  Biological process  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0006118                       electron transport       599          23    12.27               2  0.0017  0.0020 0.0017 0.0017
2   GO:0051341       regulation of oxidoreductase activity        34           4     0.70               3  0.0048  0.1755 0.0048 0.0048
3   GO:0030001                       metal ion transport        45           4     0.92               5  0.0130  0.9635 0.0130 0.0495
4   GO:0015703                       chromate transport         1           1     0.02               8  0.0205  0.9992 0.0205 0.0205
5   GO:0008152                        metabolic process      3626          84    74.27               4  0.0072 2.4e-05 0.0317 0.0486
6   GO:0007585              respiratory gaseous exchange         2           1     0.04               9  0.0406  0.4794 0.0406 0.0406
7   GO:0006811                           ion transport       127           6     2.60              10  0.0449  0.9933 0.0449 1.0000
```


E.4.6 The 500 most up-regulated genes in *A. niger* ATCC 1015

GO term over-representation results for the 500 most up-regulated and statistically significantly changed genes in *A. niger* ATCC 1015 relative to *A. niger* CBS 513.88. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS    elim  weight
1   GO:0016491                  oxidoreductase activity      1146          83    46.70               1 1.0e-08  0.0257 5.8e-06 5.7e-05
2   GO:0016616 oxidoreductase activity, acting on the C...       188          18     7.66               4 0.00059  0.0045 0.00059  0.4706
3   GO:0004096                       catalase activity        10           3     0.41               5 0.00648  0.9995 0.00648  0.0065
4   GO:0005385            zinc ion transporter activity         4           2     0.16               9 0.00939  0.9855 0.00939  1.0000
5   GO:0003824                       catalytic activity      3853         185   157.00               2 1.6e-05 4.4e-07 0.01085  0.6759
6   GO:0030693                        caspase activity         6           2     0.24              12 0.02225  0.9785 0.02225  0.0222
7   GO:0004023 alcohol dehydrogenase activity, metal io...        17           3     0.69              13 0.02975  0.7423 0.02975  0.0297
8   GO:0004024 alcohol dehydrogenase activity, zinc-dep...        17           3     0.69              14 0.02975  0.7423 0.02975  0.0297
9   GO:0004025 alcohol dehydrogenase activity, iron-dep...        17           3     0.69              15 0.02975  0.7423 0.02975  0.0297
10  GO:0004022              alcohol dehydrogenase activity        18           3     0.73              16 0.03465  0.7918 0.03465  1.0000
11  GO:0015036           disulfide oxidoreductase activity        46           5     1.87              18 0.03789  0.9975 0.03789  1.0000
12  GO:0004109         coproporphyrinogen oxidase activity         1           1     0.04              19 0.04075  0.9999 0.04075  0.0407
13  GO:0004645                    phosphorylase activity         1           1     0.04              20 0.04075  0.9986 0.04075  1.0000
14  GO:0004719 protein-L-isoaspartate (D-aspartate) O-m...         1           1     0.04              21 0.04075  0.9973 0.04075  0.0407
```

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15  GO:0005381              iron ion transporter activity         1           1     0.04              22 0.04075  0.9997 0.04075  1.0000
16  GO:0008184            glycogen phosphorylase activity         1           1     0.04              23 0.04075  0.9986 0.04075  0.0407
17  GO:0008732         L-allo-threonine aldolase activity         1           1     0.04              24 0.04075  0.9989 0.04075  0.0407
18  GO:0008941          nitric oxide dioxygenase activity         1           1     0.04              25 0.04075  0.9988 0.04075  0.0407
19  GO:0015109               chromate transporter activity         1           1     0.04              26 0.04075  0.9969 0.04075  0.0407
20  GO:0018802 2,4-dihydroxyhept-2-ene-1,7-dioate aldol...         1           1     0.04              27 0.04075  0.9989 0.04075  0.0407
21  GO:0051213                      dioxygenase activity        20           3     0.81              28 0.04562  0.6473 0.04562  1.0000
22  GO:0005506                          iron ion binding        65           6     2.65              29 0.04792  0.0271 0.04792  0.0479

##########  Cellular component  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0030288    periplasmic space (sensu ProteoBacteria)         4           2     0.11               1  0.0041  0.9996 0.0041 0.0041
2   GO:0000313                        organellar ribosome         1           1     0.03               5  0.0267  1.0000 0.0267 1.0000
3   GO:0005761                     mitochondrial ribosome         1           1     0.03               6  0.0267  1.0000 0.0267 0.0267
4   GO:0005576                       extracellular region        25           3     0.67               7  0.0275  0.8963 0.0275 0.0275

##########  Biological process  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0006118                          electron transport       599          45    25.83               1 9.1e-05  0.0013  9e-05  9e-05
2   GO:0051341       regulation of oxidoreductase activity        34           6     1.47               3  0.0029  0.2738 0.0029 0.0029
3   GO:0000041             transition metal ion transport        11           3     0.47               5  0.0101  0.6493 0.0101 0.0101
4   GO:0006829                          zinc ion transport         4           2     0.17               6  0.0105  0.9780 0.0105 1.0000
5   GO:0030001                        metal ion transport        45           6     1.94               7  0.0119  0.9001 0.0119 0.1852
6   GO:0006979                response to oxidative stress        23           4     0.99               8  0.0156  0.9249 0.0156 0.0156
7   GO:0008152                          metabolic process      3626         171   156.36               4  0.0051 4.4e-05 0.0359 0.3161
8   GO:0006800 oxygen and reactive oxygen species metab...        30           4     1.29              11  0.0382  0.8149 0.0382 1.0000
9   GO:0009069 serine family amino acid metabolic proce...        30           4     1.29              12  0.0382  0.9734 0.0382 1.0000
10  GO:0006564              L-serine biosynthetic process        18           3     0.78              13  0.0400  0.5112 0.0400 0.0400
11  GO:0015674 di-, tri-valent inorganic cation transpo...        18           3     0.78              14  0.0400  0.5181 0.0400 1.0000
12  GO:0006582                   melanin metabolic process         1           1     0.04              15  0.0431  0.9992 0.0431 0.0431
13  GO:0006826                          iron ion transport         1           1     0.04              16  0.0431  0.9996 0.0431 1.0000
14  GO:0015703                          chromate transport         1           1     0.04              17  0.0431  0.9965 0.0431 0.0431
```

E.4.7 The 1000 most up-regulated genes in *A. niger* ATCC 1015

GO term over-representation results for the 1000 most up-regulated and statistically significantly changed genes in *A. niger* ATCC 1015 relative to *A. niger* CBS 513.88. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS    elim  weight
1   GO:0016491                    oxidoreductase activity      1146         139    88.91               1 2.6e-09 0.0361 5.8e-07 0.00011
2   GO:0003824                        catalytic activity      3853         350   298.92               2 8.4e-09  1e-05 9.6e-05 0.44116
3   GO:0019131           tripeptidyl-peptidase I activity         4           3     0.31               3  0.0017 0.8412  0.0017 0.00175
4   GO:0004096                         catalase activity        10           4     0.78               7  0.0051 0.9988  0.0051 0.00514
5   GO:0046915 transition metal ion transporter activit...        10           4     0.78               8  0.0051 0.9653  0.0051 0.00514
6   GO:0017172              cysteine dioxygenase activity         2           2     0.16              10  0.0060 0.9949  0.0060 0.00601
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7   GO:0016616 oxidoreductase activity, acting on the C...       188          24    14.59              14  0.0100 0.0064  0.0100 0.40202
8   GO:0004497                       monooxygenase activity      241          28    18.70              16  0.0192 0.0460  0.0192 1.00000
9   GO:0005506                            iron ion binding       65          10     5.04              17  0.0268 0.0282  0.0268 0.02684
10  GO:0016860      intramolecular oxidoreductase activity        85          12     6.59              18  0.0300 0.6493  0.0300 0.78021
11  GO:0016861 intramolecular oxidoreductase activity, ...        67          10     5.20              19  0.0324 0.7670  0.0324 0.03240
12  GO:0004089               carbonate dehydratase activity        4           2     0.31              20  0.0324 0.9500  0.0324 0.03243
13  GO:0004351            glutamate decarboxylase activity         4           2     0.31              21  0.0324 0.9998  0.0324 0.03243
14  GO:0005179                            hormone activity        4           2     0.31              22  0.0324 0.9626  0.0324 0.03243
15  GO:0005385               zinc ion transporter activity        4           2     0.31              23  0.0324 0.9783  0.0324 1.00000
16  GO:0008442 3-hydroxyisobutyrate dehydrogenase activ...        4           2     0.31              24  0.0324 0.9960  0.0324 1.00000
17  GO:0018576           catechol 1,2-dioxygenase activity        4           2     0.31              25  0.0324 0.9762  0.0324 0.03243
18  GO:0019114               catechol dioxygenase activity        4           2     0.31              26  0.0324 0.9762  0.0324 1.00000
19  GO:0020037                                 heme binding       10           3     0.78              27  0.0369 0.9988  0.0369 0.03689
20  GO:0046906                         tetrapyrrole binding       10           3     0.78              28  0.0369 0.9988  0.0369 1.00000
21  GO:0003960            NADPH:quinone reductase activity        17           4     1.32              29  0.0378 0.0045  0.0378 0.03780
22  GO:0051213                         dioxygenase activity       20           6     1.55               6  0.0032 0.5778  0.0451 1.00000
23  GO:0016853                           isomerase activity      131          16    10.16              32  0.0454 0.7579  0.0454 1.00000
24  GO:0015082 di-, tri-valent inorganic cation transpo...       18           4     1.40              33  0.0457 0.6592  0.0457 1.00000
25  GO:0016655 oxidoreductase activity, acting on NADH ...       26           5     2.02              34  0.0465 0.0941  0.0465 0.47399
26  GO:0016829                                 lyase activity    163          19    12.65              35  0.0469 0.3686  0.0469 0.91481

##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1   GO:0016021                  integral to membrane       698          51    37.01               2 0.00386  0.0549 0.0039 0.0039
2   GO:0016020                             membrane       1079          77    57.21               1 0.00017  0.8667 0.0093 0.0093
3   GO:0030288    periplasmic space (sensu ProteoBacteria)         4           2     0.21               5 0.01559  0.9983 0.0156 0.0156
4   GO:0042597                       periplasmic space         4           2     0.21               6 0.01559  0.9983 0.0156 1.0000
5   GO:0030313                           cell envelope         6           2     0.32               7 0.03634  0.9929 0.0363 1.0000
6   GO:0044462       external encapsulating structure part         6           2     0.32               8 0.03634  0.9929 0.0363 1.0000
7   GO:0005576                  extracellular region        25           4     1.33               9 0.04006  0.9734 0.0401 0.0401

##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS    elim  weight
1   GO:0006118                    electron transport       599          71    47.53               1 0.00020  0.0020 0.00020 0.00023
2   GO:0051341       regulation of oxidoreductase activity        34           9     2.70               3 0.00099  0.3186 0.00099 0.00099
3   GO:0046439                L-cysteine metabolic process         2           2     0.16               6 0.00628  0.9941 0.00628 0.00628
4   GO:0006979                response to oxidative stress        23           6     1.82               7 0.00757  0.9241 0.00757 0.00757
5   GO:0000041              transition metal ion transport        11           4     0.87               8 0.00821  0.8241 0.00821 0.00821
```

E.4.8 All genes up-regulated in *A. niger* ATCC 1015

GO term over-representation results for all genes up-regulated and statistically significantly changed in *A. niger* ATCC 1015 relative to *A. niger* CBS 513.88. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS    elim  weight
```

1	GO:0016491	oxidoreductase activity	1146	310	217.37	1	2.5e-14	0.4774	5.9e-08	3.9e-05
2	GO:0003960	NADPH:quinone reductase activity	17	10	3.22	5	0.00031	0.5581	0.00031	0.00031
3	GO:0016616	oxidoreductase activity, acting on the C...	188	61	35.66	4	5.2e-06	0.6243	0.00088	0.00091
4	GO:0004023	alcohol dehydrogenase activity, metal io...	17	9	3.22	7	0.00172	0.9454	0.00172	0.00172
5	GO:0004024	alcohol dehydrogenase activity, zinc-dep...	17	9	3.22	8	0.00172	0.9454	0.00172	0.00172
6	GO:0004025	alcohol dehydrogenase activity, iron-dep...	17	9	3.22	9	0.00172	0.9454	0.00172	0.00172
7	GO:0005351	sugar porter activity	99	30	18.78	13	0.00417	0.9898	0.00417	0.56472
8	GO:0008733	L-arabinose isomerase activity	55	19	10.43	17	0.00444	0.8784	0.00444	0.46511
9	GO:0008106	alcohol dehydrogenase (NADP+) activity	5	4	0.95	18	0.00547	0.8922	0.00547	0.00547
10	GO:0047911	galacturan 1,4-alpha-galacturonidase act...	8	5	1.52	21	0.00819	0.9340	0.00819	0.00819
11	GO:0016705	oxidoreductase activity, acting on paire...	139	38	26.37	22	0.00935	0.3602	0.00935	1.00000
12	GO:0004316	3-oxoacyl-[acyl-carrier-protein] reducta...	18	8	3.41	23	0.01174	0.9212	0.01174	1.00000
13	GO:0015925	galactosidase activity	9	5	1.71	24	0.01556	0.7639	0.01556	0.01556
14	GO:0016893	endonuclease activity, active with eithe...	19	8	3.60	25	0.01697	0.9653	0.01697	1.00000
15	GO:0004497	monooxygenase activity	241	59	45.71	27	0.01797	0.1317	0.01797	1.00000
16	GO:0016216	isopenicillin-N synthase activity	13	6	2.47	29	0.02335	0.9738	0.02335	0.02335
17	GO:0046992	oxidoreductase activity, acting on X-H a...	13	6	2.47	30	0.02335	0.9738	0.02335	1.00000
18	GO:0046993	oxidoreductase activity, acting on X-H a...	13	6	2.47	31	0.02335	0.9738	0.02335	1.00000
19	GO:0004523	ribonuclease H activity	4	3	0.76	32	0.02337	0.9310	0.02337	0.02337
20	GO:0008240	tripeptidyl-peptidase activity	4	3	0.76	33	0.02337	0.8140	0.02337	1.00000
21	GO:0008800	beta-lactamase activity	4	3	0.76	34	0.02337	0.8408	0.02337	0.02337
22	GO:0019131	tripeptidyl-peptidase I activity	4	3	0.76	35	0.02337	0.8140	0.02337	0.02337
23	GO:0004364	glutathione transferase activity	10	5	1.90	36	0.02633	0.9273	0.02633	0.02633
24	GO:0046915	transition metal ion transporter activit...	10	5	1.90	37	0.02633	0.9818	0.02633	0.02633
25	GO:0005506	iron ion binding	65	19	12.33	38	0.02928	0.1587	0.02928	0.02928
26	GO:0003824	catalytic activity	3853	796	730.84	2	7.6e-07	0.0027	0.02988	0.87997
27	GO:0005275	amine transporter activity	87	24	16.50	39	0.03091	0.9864	0.03091	1.00000
28	GO:0005279	amino acid-polyamine transporter activit...	87	24	16.50	40	0.03091	0.9864	0.03091	1.00000
29	GO:0015171	amino acid transporter activity	87	24	16.50	41	0.03091	0.9864	0.03091	0.52810
30	GO:0015203	polyamine transporter activity	87	24	16.50	42	0.03091	0.9864	0.03091	0.52810
31	GO:0004521	endoribonuclease activity	21	8	3.98	43	0.03207	0.9116	0.03207	0.73542
32	GO:0016789	carboxylic ester hydrolase activity	79	22	14.98	44	0.03413	0.7936	0.03413	0.16376
33	GO:0004502	kynurenine 3-monooxygenase activity	2	2	0.38	45	0.03595	0.9772	0.03595	0.03595
34	GO:0004768	stearoyl-CoA 9-desaturase activity	2	2	0.38	46	0.03595	0.9996	0.03595	0.03595
35	GO:0008111	alpha-methylacyl-CoA racemase activity	2	2	0.38	47	0.03595	0.9494	0.03595	0.03595
36	GO:0008113	protein-methionine-S-oxide reductase act...	2	2	0.38	48	0.03595	0.9860	0.03595	0.03595
37	GO:0016215	CoA desaturase activity	2	2	0.38	49	0.03595	0.9996	0.03595	1.00000
38	GO:0016443	bidentate ribonuclease III activity	2	2	0.38	50	0.03595	0.8913	0.03595	0.03595
39	GO:0016888	endodeoxyribonuclease activity, producin...	2	2	0.38	51	0.03595	0.9881	0.03595	0.03595
40	GO:0017172	cysteine dioxygenase activity	2	2	0.38	52	0.03595	0.9656	0.03595	0.03595
41	GO:0005342	organic acid transporter activity	89	24	16.88	53	0.03977	0.9853	0.03977	1.00000
42	GO:0046943	carboxylic acid transporter activity	89	24	16.88	54	0.03977	0.9853	0.03977	0.76812
43	GO:0016812	hydrolase activity, acting on carbon-nit...	11	5	2.09	55	0.04089	0.8748	0.04089	0.56795

########## Cellular component #############

a	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0016021	integral to membrane	698	149	111.92	2	4.8e-06	0.9586	4.8e-06	0.1084
2	GO:0016020	membrane	1079	219	173.01	1	1.2e-07	0.9962	0.0022	0.0010
3	GO:0008290	F-actin capping protein complex	2	2	0.32	5	0.026	0.9982	0.0257	0.0257
4	GO:0009341	beta-galactosidase complex	5	3	0.80	6	0.032	0.8826	0.0318	0.0318
5	GO:0005576	extracellular region	25	8	4.01	7	0.036	0.9989	0.0357	0.0357

########## Biological process #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0006118	electron transport	599	153	115.07	1	2.7e-05	0.03	2.7e-05	3.2e-05
2	GO:0006564	L-serine biosynthetic process	18	10	3.46	2	0.00063	0.75	0.00063	0.00063
3	GO:0051341	regulation of oxidoreductase activity	34	15	6.53	4	0.00076	0.45	0.00076	0.00076
4	GO:0008643	carbohydrate transport	101	30	19.40	8	0.00683	0.99	0.00683	0.00683
5	GO:0009410	response to xenobiotic stimulus	22	9	4.23	11	0.01540	0.90	0.01540	0.01540
6	GO:0042221	response to chemical stimulus	99	27	19.02	12	0.03057	0.93	0.03057	0.65009
7	GO:0006865	amino acid transport	87	24	16.71	13	0.03518	0.98	0.03518	0.03518
8	GO:0015837	amine transport	87	24	16.71	14	0.03518	0.98	0.03518	0.59516
9	GO:0015849	organic acid transport	87	24	16.71	15	0.03518	0.98	0.03518	1.00000
10	GO:0046942	carboxylic acid transport	87	24	16.71	16	0.03518	0.98	0.03518	0.59516
11	GO:0046439	L-cysteine metabolic process	2	2	0.38	17	0.03687	0.96	0.03687	0.03687
12	GO:0000041	transition metal ion transport	11	5	2.11	18	0.04294	0.90	0.04294	0.04294
13	GO:0016042	lipid catabolic process	8	4	1.54	19	0.04917	1.00	0.04917	0.19175

Appendix F

Supplementaries for chapter 8

F.1 Model reactions

Table F.1: Proton-creating reactions of the acid-production model

pH	1.5	2	2.5	3
Citrate	CITe ⇌ CIT-e + 0.0224 H+e	CITe ⇌ CIT-e + 0.0677 H+e	CITe ⇌ CIT-e + 0.1882 H+e	CITe ⇌ CIT-e + 0.4313 H+e
Gluconate	GLCNTe ⇌ GLCNT-e + 0.0063 H+e	GLCNTe ⇌ GLCNT-e + 0.0196 H+e	GLCNTe ⇌ GLCNT-e + 0.0594 H+e	GLCNTe ⇌ GLCNT-e + 0.1663 H+e
Lactate	LACe ⇌ LAC-e + 0.0043 H+e	LACe ⇌ LAC-e + 0.0136 H+e	LACe ⇌ LAC-e + 0.0418 H+e	LACe ⇌ LAC-e + 0.1213 H+e
Acetate	ACe ⇌ AC-e + 0.0006 H+e	ACe ⇌ AC-e + 0.0018 H+e	ACe ⇌ AC-e + 0.0056 H+e	ACe ⇌ AC-e + 0.0175 H+e
Oxalate	OXALe ⇌ OXAL-e + 0.6524 H+e	OXALe ⇌ OXAL-e + 0.8611 H+e	OXALe ⇌ OXAL-e + 0.969 H+e	OXALe ⇌ OXAL-e + 1.044 H+e
Succinate	SUCCe ⇌ SUCC-e + 0.0022 H+e	SUCCe ⇌ SUCC-e + 0.0069 H+e	SUCCe ⇌ SUCC-e + 0.0214 H+e	SUCCe ⇌ SUCC-e + 0.0651 H+e
Malate	MALe ⇌ MAL-e + 0.0124 H+e	MALe ⇌ MAL-e + 0.0383 H+e	MALe ⇌ MAL-e + 0.1124 H+e	MALe ⇌ MAL-e + 0.2885 H+e

pH	3.5	4	4.5	5
Citrate	CITe ⇌ CIT-e + 0.7431 H+e	CITe ⇌ CIT-e + 1.0253 H+e	CITe ⇌ CIT-e + 1.3196 H+e	CITe ⇌ CIT-e + 1.6553 H+e
Gluconate	GLCNTe ⇌ GLCNT-e + 0.3869 H+e	GLCNTe ⇌ GLCNT-e + 0.6661 H+e	GLCNTe ⇌ GLCNT-e + 0.8632 H+e	GLCNTe ⇌ GLCNT-e + 0.9523 H+e
Lactate	LACe ⇌ LAC-e + 0.3039 H+e	LACe ⇌ LAC-e + 0.5799 H+e	LACe ⇌ LAC-e + 0.8136 H+e	LACe ⇌ LAC-e + 0.9324 H+e
Acetate	ACe ⇌ AC-e + 0.0532 H+e	ACe ⇌ AC-e + 0.151 H+e	ACe ⇌ AC-e + 0.3599 H+e	ACe ⇌ AC-e + 0.6401 H+e
Oxalate	OXALe ⇌ OXAL-e + 1.1644 H+e	OXALe ⇌ OXAL-e + 1.3909 H+e	OXALe ⇌ OXAL-e + 1.6709 H+e	OXALe ⇌ OXAL-e + 1.8659 H+e
Succinate	SUCCe ⇌ SUCC-e + 0.1821 H+e	SUCCe ⇌ SUCC-e + 0.4247 H+e	SUCCe ⇌ SUCC-e + 0.7528 H+e	SUCCe ⇌ SUCC-e + 1.0726 H+e
Malate	MALe ⇌ MAL-e + 0.5768 H+e	MALe ⇌ MAL-e + 0.8694 H+e	MALe ⇌ MAL-e + 1.1253 H+e	MALe ⇌ MAL-e + 1.4170 H+e

pH	5.5	6	6.5
Citrate	CITe ⇌ CIT-e + 1.9552 H+e	CITe ⇌ CIT-e + 2.2374 H+e	CITe ⇌ CIT-e + 2.5503 H+e
Gluconate	GLCNTe ⇌ GLCNT-e + 0.9844 H+e	GLCNTe ⇌ GLCNT-e + 0.995 H+e	GLCNTe ⇌ GLCNT-e + 0.9984 H+e
Lactate	LACe ⇌ LAC-e + 0.9776 H+e	LACe ⇌ LAC-e + 0.9928 H+e	LACe ⇌ LAC-e + 0.9977 H+e
Acetate	ACe ⇌ AC-e + 0.849 H+e	ACe ⇌ AC-e + 0.9468 H+e	ACe ⇌ AC-e + 0.9825 H+e
Oxalate	OXALe ⇌ OXAL-e + 1.9533 H+e	OXALe ⇌ OXAL-e + 1.9847 H+e	OXALe ⇌ OXAL-e + 1.9951 H+e
Succinate	SUCCe ⇌ SUCC-e + 1.4010 H+e	SUCCe ⇌ SUCC-e + 1.7033 H+e	SUCCe ⇌ SUCC-e + 1.8849 H+e
Malate	MALe ⇌ MAL-e + 1.7066 H+e	MALe ⇌ MAL-e + 1.8853 H+e	MALe ⇌ MAL-e + 1.9609 H+e

F.2 Model results

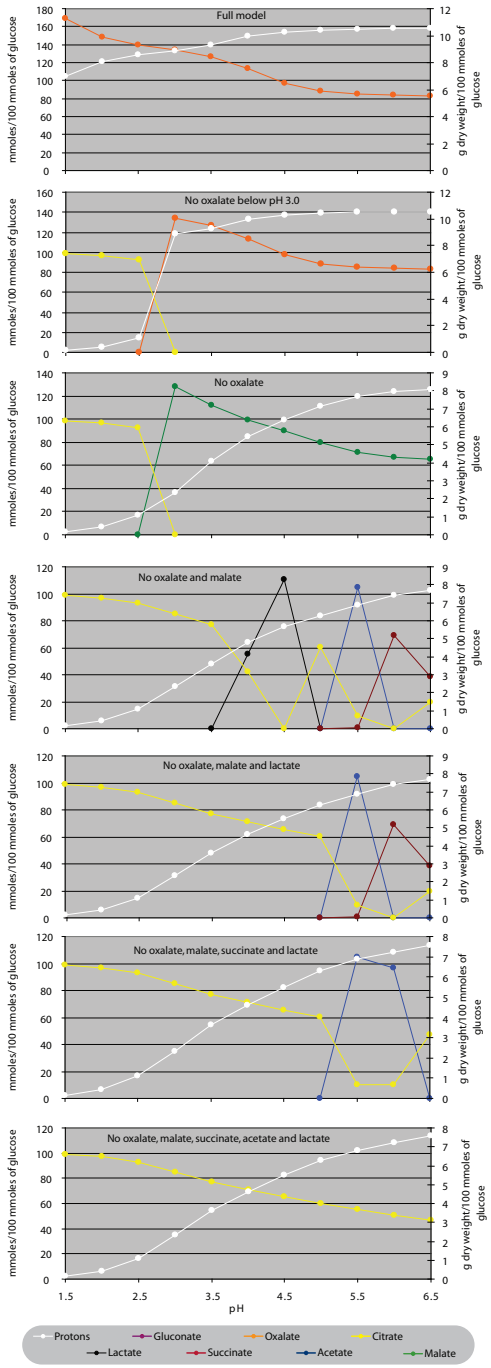

Figure F.1: Modeled acid production as a function of pH maximizing for growth coupled with acid (proton) production.

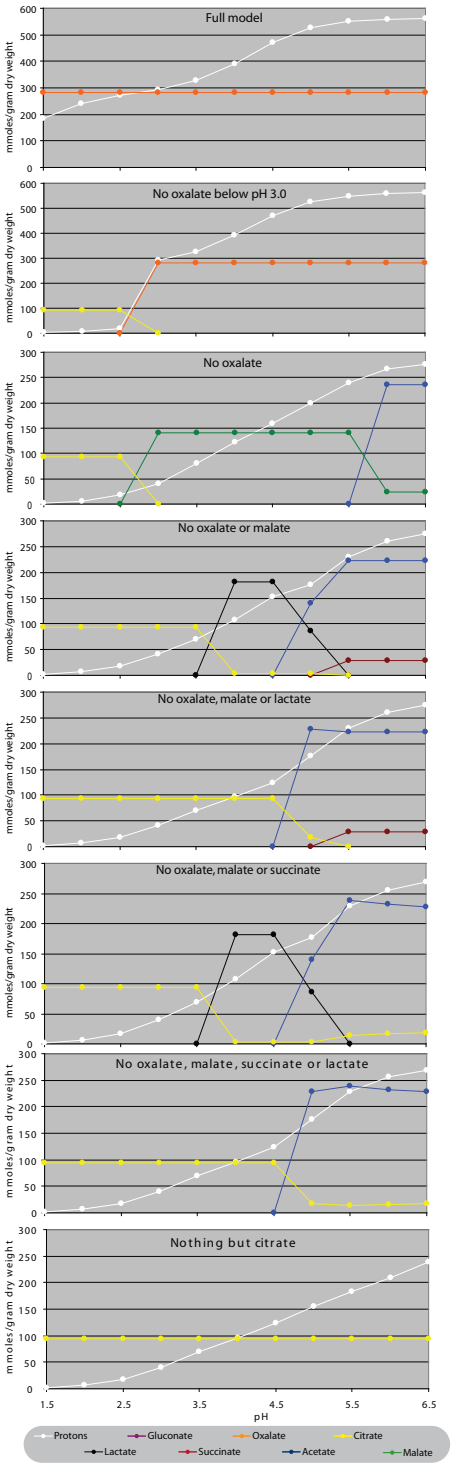

Figure F.2: Modeled acid production as a function of pH maximizing for proton production with fixed growth.

F.3 Clustering of genes

F.3.1 Graphical representation

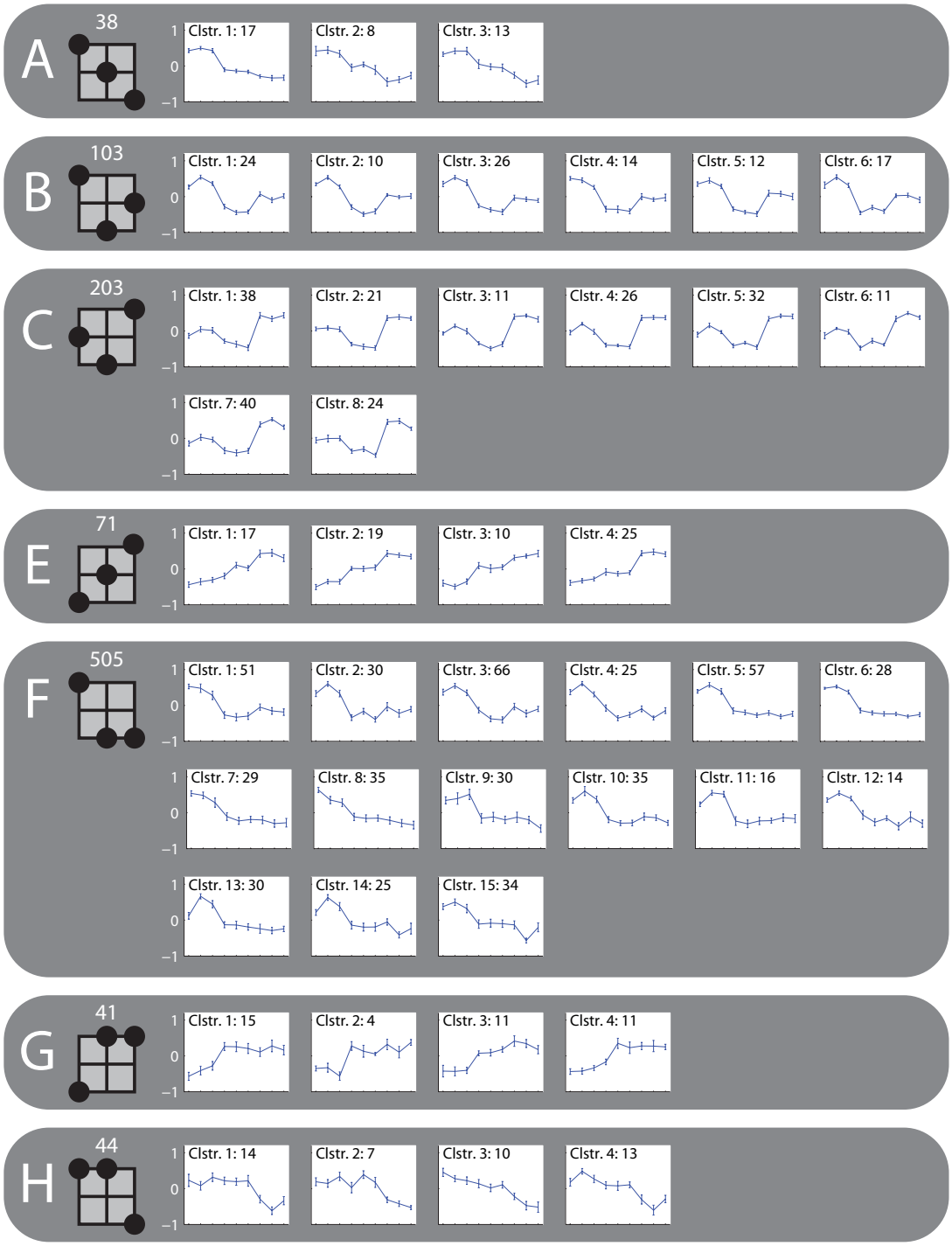

Figure F.3: Clusters A–H of genes co-regulated by ambient pH. Cluster D is not shown as it only contains one gene. The clusters are grouped based on statistical significance in pairwise comparisons of transcriptome data at pH-values 2.5, 4.5, and 6.0. Each cluster has nine values. The first three are biological replicates at pH 2.5, the middle three are at pH 4.5, and the last three are from pH 6.0. The genes are clustered using Matlab and the ClustreLustre algorithm(Grotkjaer et al., 2006).

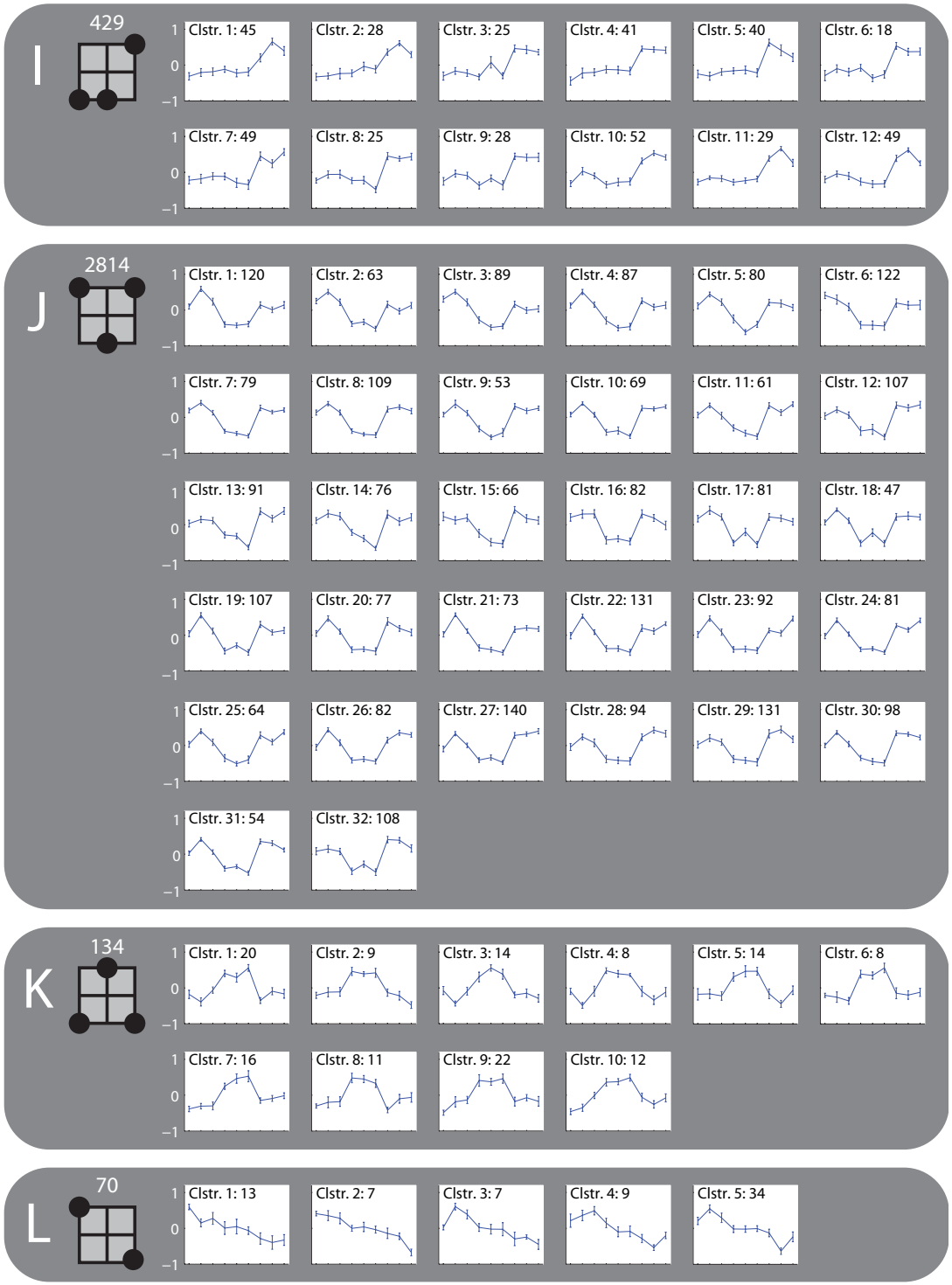

Figure F.4: Clusters I–L of genes co-regulated by ambient pH. The clusters are grouped based on statistical significance in pairwise comparisons of transcriptome data at pH-values 2.5, 4.5, and 6.0. Each cluster has nine values. The first three are biological replicates at pH 2.5, the middle three are at pH 4.5, and the last three are from pH 6.0. The genes are clustered using Matlab and the ClustreLustre algorithm(Grotkjaer et al., 2006).

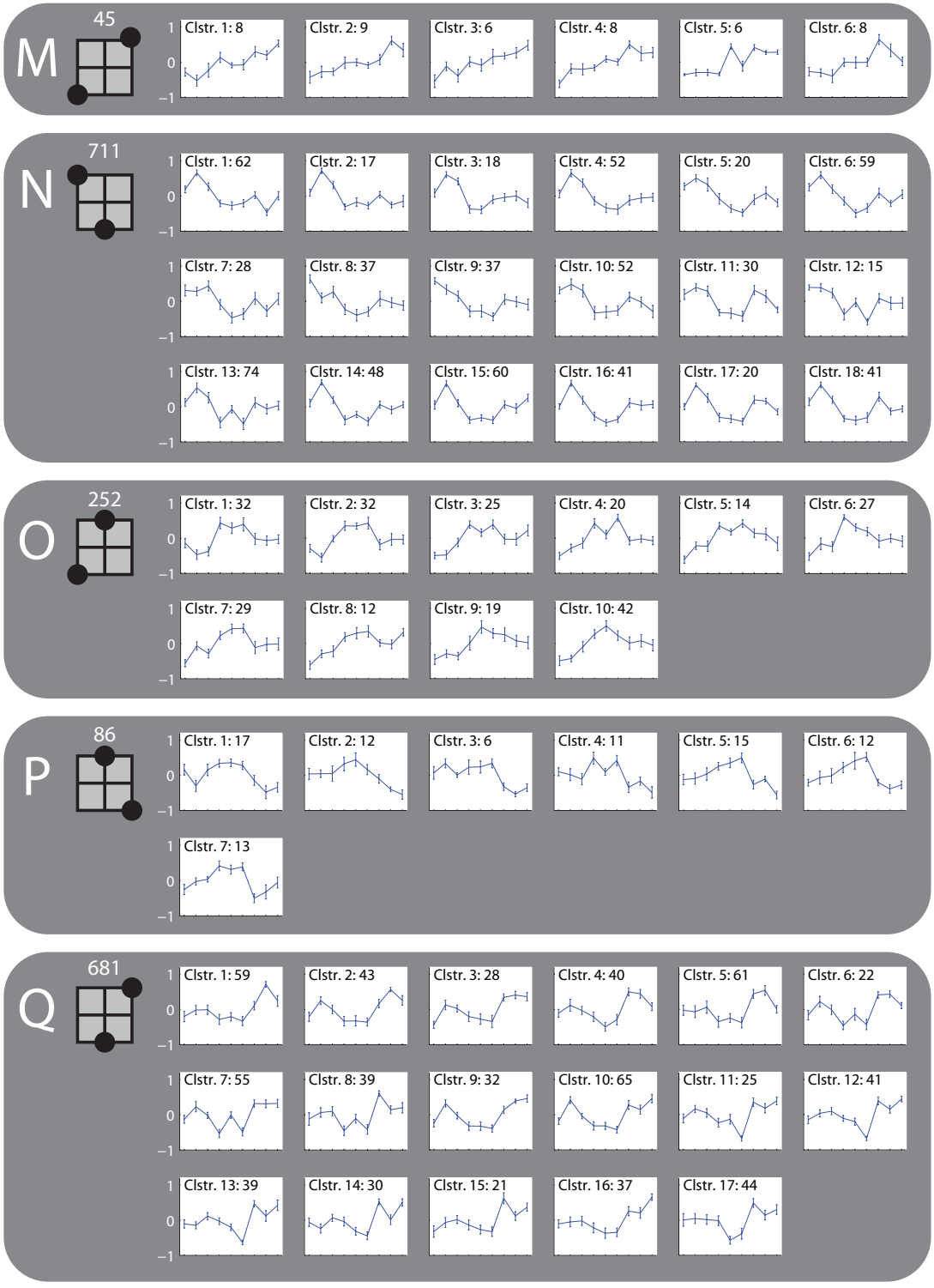

Figure F.5: Clusters M–Q of genes co-regulated by ambient pH. The clusters are grouped based on statistical significance in pairwise comparisons of transcriptome data at pH-values 2.5, 4.5, and 6.0. Each cluster has nine values. The first three are biological replicates at pH 2.5, the middle three are at pH 4.5, and the last three are from pH 6.0. The genes are clustered using Matlab and the ClustreLustre algorithm(Grotkjaer et al., 2006).

F.3.2 Table of clusters

Table F.2: Clustering of *A. niger* genes regulated by ambient pH. The HiLo, MeLo and HiMe columns are log2 ratios of gene expression indices in comparisons of pH 6.0 (Hi), pH 4.5 (Me), and pH 2.5 (Lo). Negative values mean that the index was higher in the second condition. If the comparison was not significant, a N/A is shown. The annotation column is gene-annotations as described in chapter 7. The Co-localized column: Genes with the same number are co-localized. The Sec Metabolites column: Genes that are believed to be in a co-localized, co-regulated secondary metabolite cluster are marked with numbers.

Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
A	1	212716	-4.3806	-3.2647	-1.116	hypothetical GPI anchor protein, 1,3-beta-glucanosyltransferase	scaffold_11:1540919-1542771		
A	1	57002	-3.624	-2.6188	-1.0052	hypothetical α-amylase	scaffold_12:641003-642655		
A	1	45023	-2.509	-1.785	-0.724	-	scaffold_16:227418-227926		
A	1	214718	-6.7808	-6.2666	-0.5143	Hypothetical transport protein. Belongs to the major facilitator superfamily and has 11 putative transmembrane domains	scaffold_19:463135-464598	1	
A	1	55143	-5.4819	-4.9484	-0.5335	Hypothetical dehydrogenase.	scaffold_19:465791-466945	1	
A	1	194346	-2.8602	-2.2273	-0.633	Esterase/lipase/thioesterase	scaffold_19:631321-632220	2	1
A	1	214740	-4.577	-3.0594	-1.5175	Predicted transporter (major facilitator superfamily)	scaffold_19:632462-634334	2	1
A	1	55153	-4.7428	-3.7238	-1.019	Hypothetical non-ribosomal peptide synthase	scaffold_19:635530-652452	2	1
A	1	45992	-1.9804	-1.5215	-0.4589	(chsC) Class-III chitin synthase C	scaffold_21:144575-147544		
A	1	47229	-3.4172	-2.7774	-0.6399	(phyB) phytase B	scaffold_3:258581-260204		
A	1	198750	-1.7054	-1.0479	-0.6575	Ammonium transporter	scaffold_3:2860012-2861723		
A	1	184107	-1.8535	-1.3261	-0.5274	Amino acid transporters	scaffold_7:1369686-1371596		
A	1	210776	-3.984	-2.9987	-0.9853	Amino acid/polyamine transporter I	scaffold_7:1563445-1565289		
A	1	200921	-1.7222	-1.2211	-0.5011	Permease for cytosine/purines, uracil, thiamine, allantoin	scaffold_7:272471-274154		
A	1	184195	-1.8463	-1.4214	-0.4249	putative extracellular GH 43 endo-1,5-arabinanase	scaffold_7:869299-870553		
A	1	41753	-3.5717	-3.0643	-0.5074	Hypothetical protein. Contains 6 predicted transmembrane domains	scaffold_8:899717-901144		
A	1	42307	-2.3813	-1.8181	-0.5632	Inorganic phosphate transporter	scaffold_9:838812-840867		
A	2	171927	-2.5994	-1.4755	-1.1238	related to ferro-O2-oxidoreductase	scaffold_1:1487387-1489228		
A	2	189001	-2.1875	-1.3324	-0.8551	-	scaffold_11:1465041-1466408		
A	2	213502	-1.3639	-0.6812	-0.6827	Dihydroxy-acid dehydratase	scaffold_14:332934-334559		
A	2	118750	-1.1296	-0.5443	-0.5853	putative GH family 18 endo-chitinase	scaffold_24:9107-22144		
A	2	55723	-1.4417	-0.9328	-0.5089	-	scaffold_3:1204289-1205017		
A	2	52513	-0.81	-0.444	-0.366	-	scaffold_3:288774-289897		
A	2	52530	-0.8176	-0.5092	-0.3084	-	scaffold_3:457779-458522		
A	2	201277	-1.8816	-1.1673	-0.7142	Major intrinsic protein	scaffold_7:1735722-1737293		
A	3	46809	-3.4341	-1.5025	-1.9316	Amino acid transporters	scaffold_1:3380521-3382350		
A	3	189966	-1.3688	-0.756	-0.6128	related to aspartic protease	scaffold_12:852755-854209		
A	3	127468	-1.5983	-0.8936	-0.7048	Predicted hydrolase related to dienelactone hydrolase	scaffold_13:281159-281940		
A	3	191511	-1.5417	-0.9317	-0.6101	related to GH family 12 xyloglucan-specific endo-beta-1,4-glucanase	scaffold_14:593311-594107		
A	3	214715	-3.0999	-1.4557	-1.6442	Hypothetical protein. KOG suggests chitinase. SignalP suggests secretion	scaffold_19:447259-448380		
A	3	37174	-1.0781	-0.521	-0.5572	-	scaffold_2:2390330-2390898		
A	3	207193	-1.4979	-0.7003	-0.7977	Amino acid/polyamine transporter	scaffold_2:2789984-2792230		
A	3	173997	-1.0747	-0.4759	-0.5988	Deduced translation product shares amino acid sequence identity with the Saccharomyces cerevisiae NSR1 gene product; a nucleolar protein that binds nuclear localization sequences, required for pre-rRNA processing and ribosome biogenesis.	scaffold_2:3455848-3456606		
A	3	196932	-2.5693	-1.5546	-1.0147	Esterase/lipase/thioesterase	scaffold_2:88269-89225		
A	3	182097	-1.0842	-0.5068	-0.5774	-	scaffold_6:1833339-1833560		
A	3	185564	-2.1237	-1.0634	-1.0603	Short-chain dehydrogenase/reductase SDR	scaffold_8:359204-360112		
A	3	49344	-1.538	-0.991	-0.547	putative GH family 76 endo-1,6-alpha-mannanase	scaffold_8:896926-898291		
A	3	42378	-1.5073	-0.6433	-0.864	Esterase/lipase/thioesterase	scaffold_9:1054891-1055772		
B	1	46275	-0.4745	-0.9353	0.4609	-	scaffold_1:253000-254866		
B	1	170237	-0.7806	-1.4791	0.6985	Arylacetamide deacetylase	scaffold_1:3562590-3563327		
B	1	42644	-1.3484	-2.7327	1.3843	Poly(ADP-ribose) polymerase, regulatory region	scaffold_10:226734-228945		
B	1	211797	-1.0198	-1.6985	0.6787	Hypothetical aspartic protease	scaffold_10:254815-256168		
B	1	43071	-0.8789	-1.8297	0.9508	-	scaffold_11:19388-20711		
B	1	43179	-0.9322	-1.6575	0.7253	-	scaffold_11:380998-383695		
B	1	189755	-0.5295	-1.1758	0.6462	-	scaffold_12:806560-807162		
B	1	213663	-0.3881	-0.7171	0.329	Putative ubiquitin fusion degradation protein	scaffold_15:78695-81735		
B	1	191914	-0.8683	-1.8029	0.9346	Acyl-CoA dehydrogenase,	scaffold_15:911759-913125		
B	1	214526	-0.9073	-1.9589	1.0516	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_18:378993-381026		
B	1	55114	-1.1406	-2.4284	1.2878	ATP-dependent DNA ligase	scaffold_19:103037-106066		
B	1	194178	-1.1336	-2.1453	1.0118	-	scaffold_19:459442-459666		
B	1	194417	-1.304	-2.4199	1.1159	-	scaffold_19:553980-556005		
B	1	37580	-0.6219	-1.3935	0.7716	-	scaffold_2:3779135-3780445		
B	1	46007	-0.7226	-1.1998	0.4772	-	scaffold_21:201941-202619		
B	1	47331	-0.6461	-1.5734	0.9274	Eukaryotic protein kinase domain. Related to cell cycle checkpoints	scaffold_3:843782-845460		
B	1	56022	-0.7042	-1.4964	0.7922	Cytochrome P450	scaffold_4:1787577-1789147		
B	1	180705	-0.667	-1.2267	0.5597	KU domain	scaffold_5:1103599-1106249		
B	1	40158	-0.6794	-1.2764	0.5971	Cytochrome P450	scaffold_5:2073332-2073805		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
B	1	181136	-1.0509	-2.1683	1.1174	Flavoprotein monooxygenase	scaffold_5:2321978-2323283		
B	1	48305	-1.102	-2.0263	0.9243	Isochorismatase hydrolase	scaffold_5:553448-554217		
B	1	48713	-0.7741	-1.8888	1.1148	DNA-binding SAP	scaffold_6:782917-785195		
B	1	41464	-1.0547	-1.7287	0.674	-	scaffold_8:40986-42731		
B	1	41765	-0.4935	-0.9367	0.4432	-	scaffold_8:932305-935306		
B	2	206156	-0.4277	-0.9161	0.4884	-	scaffold_1:2898963-2904970		
B	2	189637	-1.0418	-2.0864	1.0446	-	scaffold_12:442629-444909		
B	2	197291	-0.5746	-1.3028	0.7282	SNAP-25 (synaptosome-associated protein) component of SNARE complex	scaffold_2:1347244-1348558		
B	2	214840	-0.4844	-1.105	0.6206	-	scaffold_21:235462-236820		
B	2	176989	-0.6981	-1.4123	0.7142	-	scaffold_3:1664525-1666675		
B	2	48405	-0.7906	-1.9309	1.1404	-	scaffold_5:1138992-1140516		
B	2	210376	-0.4777	-1.0441	0.5664	Homocysteine S-methyltransferase	scaffold_6:1805416-1806538		
B	2	210798	-0.794	-1.7807	0.9867	Dienelactone hydrolase	scaffold_7:1725488-1726333		
B	2	49450	-0.8055	-1.5246	0.7191	Nucleic acid-binding OB-fold	scaffold_8:1537241-1537783		
B	2	56564	-0.5774	-1.1087	0.5313	Amino acid transporters	scaffold_8:659563-661273		
B	3	54128	-1.6261	-2.4077	0.7816	-	scaffold_10:615203-616566		
B	3	43260	-0.9589	-1.419	0.46	-	scaffold_11:710418-712463		
B	3	189460	-1.1132	-1.6482	0.535	ABC transporter	scaffold_12:1037715-1042530		
B	3	127335	-1.4378	-2.23	0.7922	-	scaffold_12:1141300-1142046		
B	3	213950	-0.7781	-1.245	0.467	Peptidase M28	scaffold_16:399631-401035		
B	3	57330	-0.942	-1.5682	0.6262	prtT, protease regulatory gene	scaffold_17:179061-181203		
B	3	130814	-1.1911	-2.2109	1.0198	-	scaffold_19:132268-134127		
B	3	143663	-1.0804	-1.8985	0.8181	-	scaffold_19:383185-383343	3	
B	3	55131	-1.0286	-1.5157	0.4871	-	scaffold_19:385760-386584	3	
B	3	174680	-0.522	-0.882	0.3599	candidate glucosyltransferase	scaffold_2:3452237-3454117		
B	3	37764	-1.2654	-1.7723	0.507	-	scaffold_3:359948-362191		
B	3	38995	-2.3133	-3.2604	0.9471	Hypothetical, AAA+-type ATPase domain	scaffold_4:1074558-1076476		
B	3	52980	-1.1997	-1.9209	0.7212	-	scaffold_4:1416764-1420822	4	
B	3	52981	-0.5833	-1.076	0.4927	Metacaspase involved in regulation of apoptosis	scaffold_4:1421249-1423060	4	
B	3	39105	-1.1039	-2.0026	0.8987	-	scaffold_4:1428792-1429227	4	
B	3	178969	-1.1689	-1.8311	0.6622	Major facilitator superfamily	scaffold_4:1659753-1661455		
B	3	39189	-1.6196	-2.1603	0.5408	-	scaffold_4:1680469-1681491		
B	3	143833	-1.5361	-2.2046	0.6686	Cytochrome c heme-binding site	scaffold_5:1368043-1368439		
B	3	53284	-1.6728	-2.3421	0.6694	Sugar transporter	scaffold_5:1446252-1447831		
B	3	209680	-1.3102	-2.143	0.8328	-	scaffold_5:1461600-1463506		
B	3	56215	-1.4119	-2.4003	0.9884	Hypothetical Hydroxymethylglutaryl-coenzyme A synthase	scaffold_5:1485159-1486784		
B	3	39658	-1.4237	-2.1253	0.7016	AMP-dependent synthetase and ligase	scaffold_5:308075-310022		
B	3	53233	-2.3145	-3.2491	0.9346	hypothetical short chain dehydrogenase	scaffold_5:915023-916129		
B	3	41723	-0.9521	-1.5112	0.5591	Hypothetical Cytochrome P450 monooxygenase	scaffold_8:800801-802506		
B	3	42446	-1.3599	-2.1553	0.7954	Zinc transporter ZIP	scaffold_9:1252480-1253997		
B	3	42282	-1.1744	-1.9256	0.7512	-	scaffold_9:780086-780511		
B	4	171353	-0.6107	-1.1111	0.5004	bifunctional deaminase-reductase	scaffold_1:3374570-3375400		
B	4	170954	-0.7666	-1.3705	0.6039	Transcription factor, MADS-box	scaffold_1:3669019-3669351		
B	4	189424	-1.6854	-2.2858	0.6004	putative glycosyl transferase	scaffold_12:1150547-1151628		
B	4	50744	-0.9653	-1.6396	0.6744	hypothetical glycosyl transferase family 2	scaffold_14:642570-644704		
B	4	173915	-0.5151	-0.8474	0.3324	FOG: Immunoglobin and related proteins	scaffold_2:3354516-3357940		
B	4	55790	-0.8392	-1.4095	0.5703	putative allergen produced in response to stress or pathogen infection	scaffold_3:2242459-2243554		
B	4	177220	-1.4248	-2.4628	1.038	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_3:3180371-3182303		
B	4	39372	-0.8147	-1.3391	0.5244	-	scaffold_4:2301885-2304062		
B	4	179657	-0.5415	-0.9352	0.3936	Hypothetical Major apurinic/apyrimidinic endonuclease/3’-repair diesterase APN1	scaffold_4:531302-533069		
B	4	180377	-1.0417	-1.6707	0.629	-	scaffold_5:1028104-1029007		
B	4	181664	-0.5738	-1.1966	0.6228	Large RNA-binding protein (RRM superfamily)	scaffold_5:1838784-1840362		
B	4	40867	-0.5978	-1.1835	0.5857	-	scaffold_6:1924376-1924849		
B	4	121832	-0.3763	-0.7744	0.3981	Fungal specific transcription factor	scaffold_7:1649122-1650800		
B	4	186518	-0.6501	-1.3235	0.6734	-	scaffold_9:787905-788678		
B	5	35902	-0.4165	-1.4338	1.0173	Fungal specific transcription factor	scaffold_1:1714721-1716728		
B	5	46597	-0.7122	-2.1003	1.3881	Putative Zinc transporter ZIP, Zn /Fe	scaffold_1:2048822-2049880		
B	5	43917	-0.5681	-1.2906	0.7226	Peptidase S10, serine carboxypeptidase	scaffold_12:1075101-1077031		
B	5	212940	-0.8273	-2.1584	1.3311	Hypothetical. Related to membrane bound RTA1 like protein	scaffold_12:949339-950355		
B	5	203804	-0.4976	-1.2844	0.7868	Peptidase M49	scaffold_13:1136516-1138780		
B	5	213462	-0.6899	-1.7059	1.0161	hypothetical endoglucanase	scaffold_14:270689-272334		
B	5	51199	-0.4571	-0.9446	0.4875	UMUC-like DNA-repair protein	scaffold_17:513249-515319		
B	5	173598	-0.3647	-0.9605	0.5958	-	scaffold_2:2948853-2950793		
B	5	127495	-0.8171	-1.7639	0.9468	-	scaffold_2:3495476-3495921		
B	5	208627	-0.4986	-1.1308	0.6322	M-phase inducer phosphatase (cell cycle)	scaffold_4:493556-495429		
B	5	199211	-0.4761	-1.5713	1.0952	Predicted splicing factor, SR protein superfamily	scaffold_4:841391-842812		
B	5	53539	-0.7793	-2.3181	1.5388	-	scaffold_6:1822849-1823790		
B	6	55229	-0.5669	-1.3844	0.8175	Alpha/beta hydrolase	scaffold_1:167620-168788		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
B	6	139028	-0.51	-1.0166	0.5066	Fungal specific transcription factor	scaffold_1:1863651-1865605		
B	6	139485	-0.8609	-1.6279	0.767	putative lysophospholipase with signal peptide motif	scaffold_10:211876-213716		
B	6	135939	-1.0203	-1.7576	0.7372	Hypothetical. Contains Esterase/lipase/thioesterase domain	scaffold_12:1146830-1147812		
B	6	203785	-0.8847	-1.9222	1.0375	-	scaffold_13:1081749-1082629		
B	6	55148	-0.6651	-1.1999	0.5348	-	scaffold_19:534306-534725		
B	6	194701	-0.4078	-0.7685	0.3607	-	scaffold_20:127436-127762		
B	6	55214	-0.7557	-1.506	0.7503	Hypothetical, related to kinesin	scaffold_24:102848-104218	5	
B	6	55215	-1.0556	-2.2505	1.1949	Hypothetical, related to vacuolar Ca2+/H+ antiporter VCX1	scaffold_24:106863-108183	5	
B	6	214891	-0.9981	-2.4751	1.4771	Hypothetical Calcium-Proton exchanger. Membrane bound	scaffold_24:108909-110226	5	
B	6	209752	-0.5465	-1.0935	0.547	-	scaffold_5:1671385-1673085		
B	6	128988	-1.0837	-1.9243	0.8407	Ankyrin	scaffold_5:303985-307355		
B	6	131283	-0.49	-0.8272	0.3372	hypothetical lipase	scaffold_6:1040787-1042373		
B	6	182005	-0.5404	-0.902	0.3617	Amino acid permease	scaffold_6:1806689-1808440		
B	6	183194	-0.5529	-1.0023	0.4494	hypothetical SH3 protein, which has diverse functions; KOG Class: Cell cycle control, cell division, chromosome partitioning; KOG Id: 2398; KOG description:Predicted proline-serine-threonine phosphatase-interacting protein (PSTPIP)	scaffold_7:524970-528301		
B	6	56552	-0.6534	-1.3604	0.707	Protein required for meiotic chromosome segregation	scaffold_8:507383-509771		
B	6	42292	-0.4311	-0.8184	0.3873	Flavoprotein monooxygenase	scaffold_9:801263-802662		
C	1	119500	0.5332	-0.4903	1.0235	-	scaffold_1:1141092-1144164		
C	1	205702	0.758	-0.5888	1.3467	voltage-gated potassium channel activity	scaffold_1:1328464-1329736		
C	1	51877	0.6546	-0.4571	1.1117	Isopenicillin N synthase	scaffold_1:1805762-1806975		
C	1	55365	0.6031	-0.5739	1.177	-	scaffold_1:1823715-1825494		
C	1	46621	0.7926	-0.8099	1.6025	hypothetical amylo-alpha-1,6-glucosidase. Glycogen debranching	scaffold_1:2170652-2175406		
C	1	51952	0.6002	-0.574	1.1742	-	scaffold_1:2377004-2380388		
C	1	55445	0.6229	-0.6675	1.2904	-	scaffold_1:2925925-2926846		
C	1	54081	1.1231	-0.4355	1.5586	-	scaffold_10:168426-169210		
C	1	54106	0.9572	-0.7404	1.6976	-	scaffold_10:430191-432725		
C	1	56770	0.5554	-0.492	1.0475	Peptidase S16	scaffold_10:675436-678360		
C	1	188169	0.7452	-0.4196	1.1648	Hypothetical protein kinase	scaffold_11:659606-661195		
C	1	188987	0.5254	-0.4874	1.0127	-	scaffold_11:694670-694909		
C	1	43311	0.9348	-0.5821	1.5169	hypothetical carboxylesterase	scaffold_11:845516-847645		
C	1	143560	0.7051	-0.7994	1.5045	Hypothetical, maybe secreted.	scaffold_13:1199757-1200266		
C	1	57046	0.613	-0.6187	1.2317	Aldehyde dehydrogenase	scaffold_13:532740-534542		
C	1	190212	0.5065	-0.8447	1.3512	Splicing coactivator SRm160/300, subunit SRm300	scaffold_13:568229-571798		
C	1	126405	0.613	-0.6143	1.2273	Transcription factor	scaffold_17:168183-169321		
C	1	57343	0.4808	-0.4659	0.9467	Hypothetical protein. No homology to identified proteins	scaffold_17:335707-337644		
C	1	214466	0.3993	-0.5215	0.9208	Hypothetical. KOG suggests function in ER-Golgi transport	scaffold_18:95330-97603		
C	1	207048	0.4772	-0.4225	0.8996	-	scaffold_2:2039668-2040305		
C	1	55595	1.0934	-0.3571	1.4505	G protein α subunit	scaffold_2:2367767-2369131		
C	1	174310	0.9277	-0.8132	1.7409	hypothetical protein contains SH3 adaptor domains	scaffold_2:3391676-3392658		
C	1	176664	0.5396	-0.3092	0.8488	Transcriptional activator FOSB/c-Fos and related bZIP transcription factors	scaffold_3:1931107-1932840		
C	1	55910	0.5325	-0.6925	1.225	FAD dependent oxidoreductase	scaffold_3:3567019-3569341		
C	1	55916	0.9646	-0.8953	1.8599	Hypothetical Acyl-CoA dehydrogenase	scaffold_4:163203-164900		
C	1	179224	0.613	-0.4407	1.0537	TIP120 family protein, Cullin-associated NEDD8-dissociated protein	scaffold_4:268383-271601		
C	1	130472	0.5485	-0.5247	1.0732	Fungal specific transcription factor	scaffold_4:314318-316646		
C	1	52849	0.9951	-0.6534	1.6485	-	scaffold_4:53702-54106		
C	1	209282	0.5084	-0.6521	1.1605	-	scaffold_5:148182-148681		
C	1	209363	0.6443	-0.3514	0.9956	-	scaffold_5:351149-352467		
C	1	200704	0.7306	-0.5073	1.2379	Notchless-like WD40 repeat-containing protein	scaffold_6:1152307-1154481		
C	1	182031	0.3509	-0.3147	0.6656	Non-ribosomal peptide synthetase	scaffold_6:1889639-1903109		
C	1	183511	0.8119	-0.5367	1.3486	Fungal transcriptional regulatory protein	scaffold_7:744728-746894		
C	1	53847	1.9681	-0.5903	2.5584	-	scaffold_8:1103912-1105412	6	
C	1	53848	1.2991	-0.8931	2.1922	-	scaffold_8:1106773-1107743	6	
C	1	56530	0.5758	-0.6907	1.2666	Fungal specific transcription factor	scaffold_8:258296-261949		
C	1	211539	0.7838	-0.5886	1.3724	-	scaffold_9:1006632-1008766		
C	1	49745	0.7854	-0.4939	1.2793	-	scaffold_9:1517707-1519364		
C	2	170909	0.4113	-0.7226	1.1339	Eukaryotic protein of unknown function DUF846	scaffold_1:1588346-1589114		
C	2	205951	0.3872	-0.5338	0.921	SWIB domain protein	scaffold_1:2142473-2143636		
C	2	206019	0.478	-0.7031	1.1811	-	scaffold_1:2298439-2299182		
C	2	143917	0.4723	-0.6819	1.1542	Upstream transcription factor	scaffold_1:275201-275440		
C	2	170869	0.4832	-1.0137	1.497	-	scaffold_1:3079633-3080295		
C	2	141582	0.4243	-0.4394	0.8637	Putative methyltransferase	scaffold_10:705903-706979		
C	2	50042	0.4794	-0.6941	1.1735	-	scaffold_11:254087-254516		
C	2	188549	0.3815	-0.7311	1.1126	Ubiquitin-conjugating enzymes	scaffold_11:749807-751729		
C	2	43656	0.3812	-0.4828	0.8641	-	scaffold_12:254552-256509		
C	2	192050	0.4376	-0.5806	1.0182	Hypothetical Na+:Ca2+ antiporter	scaffold_15:89794-92807		
C	2	51275	0.3137	-0.8175	1.1311	Nucleolar GTPase/ATPase	scaffold_18:238913-241097		
C	2	51355	0.5594	-0.9573	1.5167	-	scaffold_19:97523-99928		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
C	2	175118	0.48	-0.7651	1.2452	Mob1/phocein family	scaffold_2:1166738-1167842		
C	2	133787	0.8489	-1.0912	1.9401	Protein phosphatase 2C	scaffold_2:193451-194572		
C	2	174677	0.4378	-0.681	1.1188	-	scaffold_2:3718198-3720213		
C	2	47699	0.4016	-0.8825	1.2841	Membrane protein involved in ER to Golgi transport	scaffold_3:3288554-3290139		
C	2	210333	0.4115	-0.9373	1.3488	FOG: Zn-finger	scaffold_6:1657336-1660029		
C	2	184121	0.4053	-0.8685	1.2738	-	scaffold_7:206281-207495		
C	2	56471	0.5257	-0.6949	1.2205	Protein kinase	scaffold_7:946985-949222		
C	2	56526	0.5281	-0.6632	1.1913	Predicted ATPase	scaffold_8:203696-205627		
C	2	41518	0.6044	-1.1881	1.7925	-	scaffold_8:219121-221310		
C	3	190953	0.4369	-0.4241	0.861	DNA repair protein	scaffold_13:1096493-1097476		
C	3	44329	0.5445	-0.563	1.1075	Amino acid/polyamine transporter I	scaffold_13:1103864-1106225		
C	3	45152	0.413	-0.5172	0.9302	Zn-finger, C2H2 type	scaffold_16:623697-626466		
C	3	194595	0.6338	-0.8619	1.4957	Flavonol reductase/cinnamoyl-CoA reductase	scaffold_19:376513-377424		
C	3	197480	0.7479	-0.8264	1.5744	Enoyl-CoA hydratase/isomerase	scaffold_2:1832667-1833639		
C	3	173033	0.518	-0.5913	1.1093	Translation initiation factor 4F	scaffold_2:2600342-2601814		
C	3	214786	0.5925	-0.8612	1.4537	-	scaffold_20:194305-196049		
C	3	180348	0.6834	-0.7493	1.4327	Peptidase S26	scaffold_5:1801558-1804293		
C	3	210419	0.5245	-0.8141	1.3386	-	scaffold_7:208298-210545		
C	3	210989	0.3751	-0.3555	0.7305	Amino acid/polyamine transporter I	scaffold_8:470660-472501		
C	3	49311	0.8513	-0.8536	1.7049	Hypothetical, similarities to sialidase superfamily	scaffold_8:707541-708674		
C	4	205842	0.5478	-0.6133	1.1611	contains WD40 repeats	scaffold_1:1733504-1738247		
C	4	127828	0.4383	-0.661	1.0993	Microtubule-associated protein	scaffold_10:445873-446640		
C	4	54141	0.4354	-0.6814	1.1167	Ankyrin	scaffold_10:725872-729638		
C	4	50188	0.46	-0.5465	1.0065	chitin synthase D, High identity to A. nidulans chsD, Chitin-UDP acetyl-glucosaminyl transferase D, Class-V chitin synthase D	scaffold_11:1193661-1197236		
C	4	50257	0.5373	-0.8989	1.4363	-	scaffold_12:9066-10025		
C	4	44094	0.5497	-0.5764	1.1261	-	scaffold_13:384106-388425		
C	4	191378	0.5031	-0.8024	1.3056	-	scaffold_14:968731-970353		
C	4	128861	0.377	-0.789	1.166	Acyl-CoA dehydrogenase	scaffold_16:590491-596102		
C	4	193748	0.5508	-0.6127	1.1635	-	scaffold_18:377281-378406		
C	4	194208	0.3987	-0.4729	0.8716	Molybdenum cofactor biosynthesis pathway protein	scaffold_19:41688-42938	7	
C	4	45646	0.6118	-0.7321	1.344	Hypothetical 5′-3′ exonuclease	scaffold_19:46375-49767	7	
C	4	206457	0.5073	-0.7554	1.2626	-	scaffold_2:338018-339881		
C	4	173769	0.6196	-0.6689	1.2885	-	scaffold_2:3945485-3947014		
C	4	194780	0.3902	-0.9066	1.2967	-	scaffold_20:118508-119843		
C	4	45894	0.5635	-0.5183	1.0818	hypothetical protein with predicted DDT domain; KOG Class: Chromatin structure and dynamics; KOG Id: 1245; KOG Description: Chromatin remodeling complex WSTF-ISWI, large subunit (contains heterochromatin localization, PHD and BROMO domains)	scaffold_20:177488-180879		
C	4	38174	0.4623	-0.785	1.2473	-	scaffold_3:1839577-1843914		
C	4	198713	0.4904	-0.8188	1.3092	Ribonuclease II	scaffold_3:2774003-2778324		
C	4	136397	0.5431	-0.7952	1.3383	-	scaffold_3:2849613-2850802		
C	4	177806	0.5825	-0.8004	1.383	-	scaffold_3:3255607-3258157		
C	4	207663	0.6099	-0.9849	1.5948	-	scaffold_3:649787-651393		
C	4	52857	0.5011	-0.9037	1.4048	NEDD8-activating complex, APP-BP1/UBA5 component	scaffold_4:177267-179006		
C	4	39515	0.4114	-0.6354	1.0467	Ras small GTPase, Rab type	scaffold_4:2800738-2801948		
C	4	53268	0.4051	-0.6581	1.0632	Citron-like	scaffold_5:1270744-1274507		
C	4	209881	0.4999	-0.617	1.1169	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_5:2103239-2106377		
C	4	135685	0.5804	-0.6666	1.247	-	scaffold_6:2012342-2013304		
C	4	211390	0.4795	-0.5336	1.013	Transcription factor, MADS-box	scaffold_9:222598-223521		
C	5	205772	0.8237	-0.8347	1.6584	Zn-finger, C-x8-C-x5-C-x3-H type	scaffold_1:1591167-1593514		
C	5	35964	1.0189	-0.9805	1.9994	Chitin synthase	scaffold_1:1900908-1902350		
C	5	205375	0.5568	-0.6793	1.2361	SacI homology domain	scaffold_1:201210-204266		
C	5	142717	0.6692	-0.6071	1.2763	Carbohydrate kinase	scaffold_1:2193049-2194103		
C	5	55451	0.6619	-0.7199	1.3818	-	scaffold_1:2963430-2964851		
C	5	206405	0.5756	-0.6286	1.2042	Zinc-containing alcohol dehydrogenase superfamily	scaffold_1:3916209-3917560		
C	5	49922	0.6577	-0.5962	1.2539	-	scaffold_10:1200331-1201300		
C	5	188168	0.4526	-0.4754	0.928	-	scaffold_11:32320-32922		
C	5	54326	0.5912	-0.4928	1.084	Related to S. cerevisiae glutamine-dependent NAD synthetase (EC 6.3.5.1)	scaffold_11:361718-364580		
C	5	50071	0.5684	-0.4567	1.0251	Hypothetical (stress responsive ?)	scaffold_11:411839-412273	8	
C	5	143341	0.5943	-0.4811	1.0755	-	scaffold_11:414176-414724	8	
C	5	128744	0.6184	-0.7238	1.3422	-	scaffold_12:323455-328617		
C	5	213358	0.5956	-0.8101	1.4057	Fungal specific transcription factor	scaffold_13:1109702-1111759		
C	5	213051	0.4583	-0.5953	1.0537	Hypothetical Aldose 1-epimerase	scaffold_13:263635-264760		
C	5	54557	0.6581	-0.7461	1.4042	-	scaffold_13:361927-363132		
C	5	192461	0.4223	-0.6379	1.0602	-	scaffold_16:484068-486014		
C	5	204687	0.5022	-0.5071	1.0093	Fungal transcriptional regulatory protein, N-terminal	scaffold_17:239013-241452		
C	5	204764	0.699	-0.6312	1.3303	-	scaffold_17:467295-469140		
C	5	52207	0.5451	-0.7228	1.2679	-	scaffold_2:1130708-1132111		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
C	5	52215	0.5535	-0.7307	1.2842	-	scaffold_2:1226013-1227653		
C	5	206812	0.5566	-0.6472	1.2038	-	scaffold_2:1413506-1414983		
C	5	47034	0.4364	-0.3276	0.764	-	scaffold_2:1864239-1866223		
C	5	174067	0.5762	-0.6345	1.2107	-	scaffold_2:455551-456853		
C	5	208486	0.5296	-0.5699	1.0995	Peptidase S10	scaffold_3:3524172-3528044		
C	5	177282	0.62	-0.7227	1.3427	-	scaffold_3:782610-783630		
C	5	198250	0.722	-0.7325	1.4545	2-enoyl-CoA hydratase/3-hydroxyacyl-CoA dehydrogenase/Peroxisomal 3-ketoacyl-CoA-thiolase, sterol-binding domain and related enzymes	scaffold_3:893653-894178		
C	5	52947	0.4794	-0.4814	0.9608	Peptidase C19	scaffold_4:1144474-1148117		
C	5	48160	0.5934	-0.5454	1.1388	Hypothetical protein. HMMPfam indicates Acyl-CoA dehydrogenase activity.	scaffold_4:2682858-2684390		
C	5	178675	0.6772	-0.7654	1.4426	Autophagy protein Apg4, cystein proteinas	scaffold_4:2924796-2926255		
C	5	40551	0.5089	-0.4041	0.913	-	scaffold_6:909860-911093		
C	5	41388	0.6452	-0.6537	1.2989	Actin regulatory proteins	scaffold_7:1610428-1611600		
C	5	56629	0.4508	-0.6854	1.1362	cullin 4 type protein	scaffold_8:1550449-1559194		
C	6	35778	0.459	-0.484	0.943	Hypothetical long chain fatty alcohol oxidase	scaffold_1:1321485-1323832		
C	6	212116	0.5101	-0.4391	0.9492	-	scaffold_10:1198384-1200023		
C	6	55218	0.9819	-0.955	1.9369	-	scaffold_124:107-604		
C	6	213237	0.9606	-0.6117	1.5723	-	scaffold_13:792539-795464		
C	6	55052	0.9991	-0.4274	1.4265	Fungal specific transcription factor	scaffold_18:84724-87532		
C	6	36874	0.3838	-0.4859	0.8697	(pkaC) cAMP-dependent protein kinase catalytic subunit	scaffold_2:1110116-1111751		
C	6	37444	0.5795	-0.4468	1.0263	Predicted cation transporter	scaffold_2:3371254-3372493		
C	6	199609	0.7185	-0.7001	1.4186	hypothetical protein containing fungal specific transcription factor and fungal transcriptional regulatory protein domains.	scaffold_4:2679493-2681928		
C	6	39573	0.4802	-0.3233	0.8035	-	scaffold_5:38997-40574		
C	6	56354	0.5345	-0.4024	0.9369	putative cyclin, possible interaction with ASN134471	scaffold_6:1523006-1524025		
C	6	53949	0.4518	-0.3517	0.8035	Major facilitator superfamily	scaffold_9:311243-313403		
C	7	172439	1.1825	-0.3608	1.5432	-	scaffold_1:1447747-1448214		
C	7	35601	0.4731	-0.385	0.8581	-	scaffold_1:803122-803525		
C	7	119238	1.2431	-0.7286	1.9717	Fungal Zn(2)-Cys(6) binuclear cluster domain	scaffold_10:462293-465827		
C	7	56782	3.6521	-0.741	4.3931	Glycosyl hydrolase family 3 C terminal domain	scaffold_10:813052-815999		
C	7	202494	0.8827	-0.4427	1.3253	Predicted E3 ubiquitin ligase	scaffold_10:982814-984206		
C	7	188673	0.5813	-0.375	0.9563	AMP-dependent synthetase and ligase	scaffold_11:51693-54034		
C	7	203398	0.8681	-0.5934	1.4615	Acyltransferase 3	scaffold_12:1051173-1052591		
C	7	190311	0.8022	-0.8441	1.6463	2-nitropropane dioxygenase	scaffold_13:599152-600192		
C	7	57197	0.5002	-0.4984	0.9986	Glutathione-dependent formaldehyde-activating, GFA	scaffold_15:162563-163615		
C	7	50837	0.6218	-0.4851	1.107	Hypothetical. Peroxisomal pex2/pex12. Zn finger	scaffold_15:197342-198478		
C	7	191932	0.5624	-0.3953	0.9577	Major facilitator superfamily	scaffold_15:899179-900733		
C	7	122135	0.542	-0.4897	1.0316	-	scaffold_16:353079-354536		
C	7	214348	0.9606	-0.925	1.8856	Acyl-CoA synthetase	scaffold_17:490915-493229		
C	7	45434	0.9894	-0.7536	1.7429	Glycerol kinase (glcA).	scaffold_17:666990-668890		
C	7	45270	0.4765	-0.47	0.9465	-	scaffold_17:82308-84148		
C	7	193642	0.6548	-0.4723	1.1271	-	scaffold_18:51958-53777		
C	7	45789	0.5137	-0.3932	0.9068	hypothetical copper amine oxidase	scaffold_19:456774-458973		
C	7	206922	0.9163	-0.4201	1.3363	Tomosyn and related SNARE-interacting proteins	scaffold_2:1697656-1702805		
C	7	130834	1.0939	-0.5705	1.6644	Fungal specific transcription factor	scaffold_2:2536247-2538483		
C	7	52344	0.9015	-0.5245	1.426	-	scaffold_2:2547551-2548351		
C	7	206534	0.7767	-0.8259	1.6026	Zinc-binding oxidoreductase	scaffold_2:540794-541959		
C	7	194767	0.7389	-0.5014	1.2403	-	scaffold_20:154387-155283		
C	7	194806	1.0714	-0.7085	1.78	Fungal specific transcription factor	scaffold_20:227406-229957		
C	7	207853	1.3551	-0.7625	2.1176	Predicted dehydrogenase	scaffold_3:1561579-1562900		
C	7	139020	0.9373	-0.4221	1.3594	(facB) Acetate regulatory gene. Also known as acuB. Homologue of the A. nidulans facB	scaffold_3:1884535-1887399		
C	7	177847	1.0127	-1.0232	2.0358	ABC transporter	scaffold_3:2077008-2079329		
C	7	176015	1.3342	-0.6007	1.9349	-	scaffold_3:2155602-2156585		
C	7	207710	0.599	-0.4825	1.0814	MAP kinase	scaffold_3:745209-746424		
C	7	199510	0.7508	-0.5644	1.3153	Sugar transporter superfamily	scaffold_4:2453124-2455510		
C	7	208716	0.6364	-0.3541	0.9905	Fungal specific transcription factor	scaffold_4:809205-812446		
C	7	53278	0.7837	-0.852	1.6357	-	scaffold_5:1398692-1400580		
C	7	39988	1.2558	-0.8865	2.1423	-	scaffold_5:1467334-1471409		
C	7	209685	0.7453	-0.6571	1.4024	Acyl-CoA dehydrogenase	scaffold_5:1480175-1481776		
C	7	181551	0.6206	-0.5155	1.1361	GPCR, family 2, secretin-like	scaffold_5:1790101-1791822		
C	7	181179	1.0423	-0.5517	1.594	Catechol dioxygenase, N-terminal	scaffold_5:822172-823280		
C	7	181735	0.7941	-0.4821	1.2762	Fungal specific transcription factor	scaffold_6:742554-744826		
C	7	181888	0.7114	-0.4616	1.1731	Carboxyl transferase	scaffold_6:817292-819100		
C	7	48950	0.7383	-0.6648	1.4031	AAA ATPase	scaffold_7:353238-357044		
C	7	201122	1.2738	-0.4847	1.7584	-	scaffold_7:802743-803791		
C	7	42065	0.5701	-0.4775	1.0476	-	scaffold_9:110779-111954		
C	8	170910	0.5259	-0.5374	1.0633	Glucose/ribitol dehydrogenase	scaffold_1:1110269-1111463		
C	8	55356	0.5889	-0.371	0.96	Glucose-repressible alcohol dehydrogenase transcriptional effector CCR4 and related proteins	scaffold_1:1673092-1675402		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
C	8	35474	0.7143	-0.4201	1.1344	Hypothetical WD40 repeat-containing protein involved in peroxisomal matrix import.	scaffold_1:349118-350244		
C	8	55261	0.6889	-0.6262	1.3151	-	scaffold_1:549338-550902		
C	8	202548	0.497	-0.3254	0.8224	Signaling protein SWIFT and related BRCT domain proteins	scaffold_10:1120592-1125405		
C	8	187949	0.8479	-0.6457	1.4936	Esterase/lipase/thioesterase	scaffold_10:1948296-1949249		
C	8	211917	0.98	-1.0486	2.0286	Dual specificity phosphatase, catalytic domain	scaffold_10:691002-693312		
C	8	189537	0.3866	-0.3098	0.6963	Acyl-CoA synthetase	scaffold_12:340484-342619		
C	8	212893	1.2739	-0.8635	2.1374	Glycoside hydrolase	scaffold_12:490705-493454		
C	8	191450	0.7199	-0.4381	1.1581	-	scaffold_14:135023-135938		
C	8	45070	0.8457	-0.7763	1.622	-	scaffold_16:358826-359745		
C	8	52201	0.4766	-0.3778	0.8545	Cdc4 and related F-box and WD-40 proteins	scaffold_2:1070583-1072772		
C	8	119171	0.6633	-0.4714	1.1347	-	scaffold_2:207315-210815		
C	8	52839	0.4327	-0.3763	0.809	-	scaffold_3:3534436-3536767		
C	8	52536	0.4662	-0.3351	0.8013	Ubiquitin-conjugating enzyme	scaffold_3:503629-504418		
C	8	176142	0.4032	-0.3453	0.7485	1-aminocyclopropane-1-carboxylate synthase, and related proteins	scaffold_3:703112-704750		
C	8	119885	0.4565	-0.4232	0.8797	Zn-finger, GATA type	scaffold_4:2796121-2798642		
C	8	208679	0.5321	-0.571	1.103	-	scaffold_4:688737-691905		
C	8	56146	0.3899	-0.4569	0.8467	-	scaffold_5:474664-476127		
C	8	209490	0.4743	-0.6067	1.081	GH family 76	scaffold_5:706290-708149		
C	8	39803	0.9396	-0.7589	1.6984	Yippee-type zinc-binding protein	scaffold_5:849029-849428		
C	8	41300	0.4119	-0.3521	0.7641	AAA ATPase	scaffold_7:1347551-1352004		
C	8	183742	0.4754	-0.3723	0.8477	Fungal specific transcription factor	scaffold_7:1599900-1602217		
C	8	210597	0.4586	-0.538	0.9966	cAMP-dependent protein kinase	scaffold_7:631349-632584		
D	1	50973	0.3658	0.7465	-0.3806	putative extracellular tannase and feruloyl esterase	scaffold_16:243444-245189		
E	1	188883	4.2475	1.4089	2.8386	Alpha-amylase	scaffold_11:1440474-1442598	9	
E	1	54411	1.599	0.5142	1.0848	Short-chain dehydrogenase/reductase SDR	scaffold_11:1443391-1444419	9	
E	1	43565	2.2013	0.8458	1.3555	-	scaffold_11:1622460-1624193		
E	1	43746	2.1599	0.8247	1.3352	hypothetical ribonuclease T1	scaffold_12:559123-559937		
E	1	191223	0.9367	0.3441	0.5926	Amino acid/polyamine transporter II	scaffold_14:553721-555453		
E	1	54812	4.2412	1.9456	2.2956	putative extracellular protein	scaffold_15:404979-405629		
E	1	57241	6.3807	3.9334	2.4472	oahA, Oxaloacetate acetylhydrolase oahA (EC 3.7.1.1)	scaffold_16:211445-212676		
E	1	214527	2.5257	1.0805	1.4453	Dihydrodipicolinate synthetase family	scaffold_18:398853-399791		
E	1	36572	2.3804	1.1156	1.2648	Peptidase M	scaffold_2:3263-7998		
E	1	38982	1.553	0.6153	0.9378	AAA ATPase	scaffold_4:1030328-1032602		
E	1	39278	3.3448	1.7031	1.6417	Inorganic ion transport and metabolism	scaffold_4:1998457-2000717		
E	1	48891	2.112	1.0713	1.0407	putative extracellular protein	scaffold_6:1887108-1887767		
E	1	128747	1.1575	0.5048	0.6527	putative GH family 18 endo-chitinase	scaffold_6:2013696-2019569		
E	1	200589	1.5807	0.8315	0.7492	8-amino-7-oxononanoate synthase (biotin synthesis)	scaffold_6:638240-639643		
E	1	184740	0.7205	0.3562	0.3643	Transcription elongation factor	scaffold_8:1228234-1229201		
E	1	41900	4.4434	2.2729	2.1705	-	scaffold_8:1350890-1352491		
E	1	186088	1.7535	1.0142	0.7393	-	scaffold_9:431755-432498		
E	2	188056	3.214	1.8773	1.3367	Cytochrome P450	scaffold_10:591436-593141	10	2
E	2	54123	4.1629	2.4376	1.7252	-	scaffold_10:594381-597263	10	2
E	2	54125	1.9878	1.0914	0.8965	-	scaffold_10:600682-602004	10	2
E	2	54126	1.9298	1.1624	0.7674	Cytochrome P450	scaffold_10:603085-604954	10	2
E	2	42759	2.3108	1.1968	1.114	-	scaffold_10:606816-608003	10	2
E	2	188489	2.8198	1.6331	1.1867	Alpha amylase	scaffold_11:1000471-1002186		
E	2	191085	0.7887	0.3871	0.4017	-	scaffold_13:81774-83498		
E	2	44605	0.9388	0.5794	0.3594	Putative fungal transcriptional regulatory protein. May be erroneously joined with ribosomal protein S2.	scaffold_14:827490-829007		
E	2	50898	3.1579	1.9355	1.2224	Hypothetical permease. 10 predicted transmembrane domains. May have Xanthine/uracil transporter activity	scaffold_15:591485-593355		
E	2	54896	1.8228	0.8816	0.9413	-	scaffold_16:553754-555501		
E	2	204783	1.4072	0.6385	0.7687	Hypothetical ADAM ("a disintegrin and metalloprotease")family gene	scaffold_17:516241-518444		
E	2	207278	4.1674	1.8003	2.3671	-	scaffold_2:3175870-3176841	11	
E	2	197780	4.2184	2.5182	1.7002	hypothetical protein containing aspartic protease active site	scaffold_2:3180601-3182745	11	
E	2	181376	1.5283	0.8049	0.7234	Ferric reductase-like transmembrane component	scaffold_5:1198206-1200194	12	
E	2	137643	2.0506	0.9689	1.0817	Hypothetical copper transporter	scaffold_5:1200452-1200999	12	
E	2	183355	2.7034	1.2222	1.4813	Histidine acid phosphatase	scaffold_7:1423774-1425159		
E	2	183274	0.9389	0.5876	0.3512	TatD-related DNase	scaffold_7:1685266-1686270		
E	2	41698	0.8815	0.3755	0.5061	Sugar transporter	scaffold_8:725685-727344		
E	2	202078	3.8296	2.1098	1.7198	Amino acid permease	scaffold_9:1228865-1230783		
E	3	55494	4.2152	2.3934	1.8218	homologue of the catalase catB gene of Aspergillus oryzae and Aspergillus fumigatus	scaffold_1:3476979-3479451		
E	3	52071	2.2404	1.9079	0.3325	Endo-1,4-beta-xylanase II precursor (Xylanase II) (1,4-beta-D-xylan xylanohydrolase II)	scaffold_1:3754017-3754762		
E	3	131352	2.5632	1.7157	0.8475	Multicopper oxidases	scaffold_10:588881-590657		
E	3	43221	2.2639	1.3616	0.9023	Amino acid transporters	scaffold_11:532543-534238		
E	3	57285	2.1215	1.4163	0.7052	Major facilitator superfamily	scaffold_16:719023-720812		
E	3	45425	0.633	0.3192	0.3138	Glycosylphosphatidylinositol anchor synthesis protein	scaffold_17:618126-620950		
E	3	47117	1.2077	0.5357	0.672	related to ACC synthase	scaffold_2:3114533-3115834		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
E	3	52107	0.7926	0.4164	0.3762	Chitinase	scaffold_2:90107-90915		
E	3	195023	1.1964	0.5479	0.6485	-	scaffold_21:49806-50930		
E	3	140924	2.3973	1.5777	0.8196	-	scaffold_9:627485-628940		
E	4	46428	2.729	0.476	2.253	Major facilitator superfamily	scaffold_1:1165930-1167818		
E	4	51930	2.537	0.8352	1.7019	Gen A8; hypothetical Cyanovirin-N protein	scaffold_1:2206197-2206614		
E	4	52061	2.295	0.8652	1.4297	Glycosyl hydrolase family 65	scaffold_1:3479804-3483162		
E	4	196874	3.079	0.5382	2.5408	Aldehyde dehydrogenase	scaffold_1:3792969-3794527		
E	4	54127	1.4704	0.4336	1.0368	-	scaffold_10:605231-606309		
E	4	212736	4.1784	1.4875	2.6909	aglC, α-galactosidase; degradation of melibiose; EC 3.2.1.22; SwissProt ID AGALC_ASPNG; secreted α-galactosidase	scaffold_11:1638103-1640476		
E	4	189206	4.1	1.0759	3.0241	-	scaffold_11:296049-297402		
E	4	204301	2.5332	0.7127	1.8205	candidate 1,3-beta-glucanosyltransferase	scaffold_16:98218-99664		
E	4	194165	1.3059	0.4783	0.8276	unknown. Signal P suggests Anchor	scaffold_19:507728-509216		
E	4	125698	3.6662	1.4636	2.2026	-	scaffold_2:1007838-1008543		
E	4	47049	3.0304	0.9391	2.0913	pacC	scaffold_2:1994287-1996482		
E	4	207276	2.9604	0.9512	2.0093	UDP-glucose 4-epimerase	scaffold_2:3167099-3168385		
E	4	52406	2.2982	0.6905	1.6077	Beta-ketoacyl synthase	scaffold_2:3185712-3194240		
E	4	173507	2.135	0.4597	1.6753	Glycosyl hydrolase family 76	scaffold_2:691253-692839		
E	4	205168	2.9416	0.6024	2.3392	Sulfatase	scaffold_20:5215-7909		
E	4	38152	1.5604	0.385	1.1754	-	scaffold_3:1739982-1741007		
E	4	39867	1.032	0.3789	0.6532	-	scaffold_5:1049232-1049654		
E	4	210306	2.7211	0.3465	2.3746	Hypothetical aspartic protease	scaffold_6:1577756-1579145		
E	4	41247	1.404	0.5943	0.8097	-	scaffold_7:1128093-1129442		
E	4	41165	3.711	1.2555	2.4555	putative GH family 16 GPI_glucanosyltransferase	scaffold_7:845138-846296		
E	4	53760	0.7813	0.299	0.4822	Glucose/ribitol dehydrogenase	scaffold_8:394486-395542		
E	4	56566	5.9182	0.5819	5.3363	Major facilitator superfamily	scaffold_8:689801-692738		
E	4	186595	1.6593	0.6381	1.0212	-	scaffold_9:1613368-1614903		
E	4	42166	2.2206	0.4506	1.77	Ferric reductase, NADH/NADPH oxidase and related proteins	scaffold_9:437241-439330		
E	4	186792	1.887	0.5461	1.341	-	scaffold_9:745658-747381		
F	1	143936	-0.8094	-1.1098	N/A	DNA directed RNA polymerase	scaffold_1:1906166-1906315		
F	1	172416	-0.7742	-1.1337	N/A	Major facilitator superfamily	scaffold_1:3413437-3414976		
F	1	36404	-1.3614	-1.4859	N/A	FAD linked oxidase, N-terminal	scaffold_1:3503911-3505723		
F	1	142713	-0.672	-0.9197	N/A	putative lysophospholipase/carboxylesterase family protein	scaffold_1:3678095-3678877		
F	1	170255	-0.4547	-0.5755	N/A	Eukaryotic glutathione synthase	scaffold_1:368432-370042		
F	1	54077	-0.5851	-0.8288	N/A	Major intrinsic protein	scaffold_10:139090-141549		
F	1	187796	-1.4079	-1.9793	N/A	-	scaffold_10:249120-250294		
F	1	42787	-0.4194	-0.5134	N/A	-	scaffold_10:708277-710469		
F	1	42843	-0.5365	-0.7739	N/A	Fungal transcriptional regulatory protein	scaffold_10:921417-922472		
F	1	124700	-0.6103	-0.7677	N/A	Esterase/lipase/thioesterase	scaffold_11:1477771-1478838		
F	1	125408	-1.7366	-2.0108	N/A	Glycan biosynthesis	scaffold_12:1149452-1150467		
F	1	190797	-0.4006	-0.5671	N/A	acid phosphatase	scaffold_13:534784-536428		
F	1	213572	-0.8382	-1.079	N/A	Hypothetical. Related to cell surface antigen spherulin	scaffold_14:598203-599329		
F	1	50755	-0.795	-0.9334	N/A	putative RTA1 like protein	scaffold_14:721965-722927		
F	1	127602	-0.693	-1.0276	N/A	β-1,6-N-acetylglucosaminyltransferase	scaffold_15:119534-120222		
F	1	125140	-2.5286	-2.9728	N/A	-	scaffold_15:934268-935161		
F	1	192646	-0.4084	-0.5506	N/A	Sybindin-like protein	scaffold_16:781132-781679		
F	1	193160	-0.4844	-0.6324	N/A	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_17:264520-265473		
F	1	51186	-1.0546	-1.4893	N/A	HMG-box transcription factor	scaffold_17:427090-429285		
F	1	127007	-0.402	-0.5122	N/A	Hypothetical DnaJ domain protein, mitochondrial	scaffold_18:247272-247829		
F	1	214608	-1.3271	-1.8876	N/A	candidate endo-1,4-beta-glucanase; glucan 1,4-beta-glucosidase; glycoside hydrolase, family 5; cellulose-binding region, fungal	scaffold_18:607627-609397		
F	1	45631	-1.292	-1.316	N/A	Ankyrin	scaffold_18:661275-664778		
F	1	194300	-1.7152	-2.5099	N/A	candidate Ribonuclease III	scaffold_19:445143-445567		
F	1	172934	-0.7823	-1.2583	N/A	ABC transporter	scaffold_2:1248848-1251134		
F	1	55614	-0.7266	-0.8605	N/A	GNS1/SUR4 membrane protein	scaffold_2:2813808-2814954		
F	1	207490	-0.8289	-1.1691	N/A	Carboxylesterases	scaffold_2:3856167-3858257		
F	1	45867	-0.6153	-0.722	N/A	-	scaffold_20:97487-102444		
F	1	127803	-0.4841	-0.785	N/A	Ankyrin	scaffold_3:1038332-1038757	13	
F	1	207785	-0.9311	-1.1326	N/A	Kinesin light chain	scaffold_3:1041921-1044901	13	
F	1	177781	-0.8681	-0.9119	N/A	GCN5-related N-acetyltransferase	scaffold_3:1188622-1189204		
F	1	52700	-1.0464	-1.2545	N/A	related to extracellular tripeptidyl peptidase	scaffold_3:2327525-2329456		
F	1	138144	-0.4277	-0.6085	N/A	Ribosomal L32p protein	scaffold_3:3549828-3550152		
F	1	176195	-1.1971	-1.284	N/A	AMP-dependent synthetase and ligase	scaffold_3:515250-517029		
F	1	178726	-1.0206	-1.4794	N/A	-	scaffold_4:1333652-1334589		
F	1	209127	-0.4762	-0.7674	N/A	-	scaffold_4:2695323-2696654		
F	1	52874	-1.2263	-1.5795	N/A	Serine/threonine protein kinase	scaffold_4:353736-356199		
F	1	180728	-0.4744	-0.7671	N/A	-	scaffold_5:1063957-1064943		
F	1	56242	-0.4649	-0.5903	N/A	-	scaffold_5:1821658-1822809		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
F	1	180332	-0.4369	-0.7472	N/A	hypothetical β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_5:1842595-1843818		
F	1	40206	-1.291	-1.5038	N/A	Hypothetical glutathione S-transferase	scaffold_5:2211877-2212655		
F	1	123881	-0.7501	-1.0615	N/A	-	scaffold_5:813581-814829		
F	1	183088	-1.2207	-1.3059	N/A	hypothetical xylanase	scaffold_6:1179006-1179771		
F	1	40791	-0.474	-0.5357	N/A	-	scaffold_6:1654222-1655017		
F	1	183962	-0.3756	-0.5754	N/A	-	scaffold_7:1301745-1303070		
F	1	41358	-0.3878	-0.445	N/A	Predicted Ca2+-modulated nonselective cation channel	scaffold_7:1524107-1525249		
F	1	183780	-0.7581	-1.0334	N/A	-	scaffold_7:898436-900087		
F	1	53849	-1.1192	-1.2063	N/A	-	scaffold_8:1123215-1124738		
F	1	184509	-1.2311	-1.4578	N/A	Hypothetical methyltransferase. No sequence similarity is found to identified proteins	scaffold_8:1388626-1389872		
F	1	201345	-0.8098	-0.9376	N/A	Transcription factor PRD and related proteins	scaffold_8:147439-149354		
F	1	42462	-0.3239	-0.4393	N/A	-	scaffold_9:1305867-1306352		
F	1	42044	-0.6683	-0.953	N/A	-	scaffold_9:57898-58332		
F	2	172523	-0.4785	-0.6271	N/A	Coenzyme A transferase	scaffold_1:3124164-3125994		
F	2	139486	-0.6565	-0.9666	N/A	Esterase/lipase/thioesterase	scaffold_1:3552911-3554848		
F	2	187977	-1.1708	-1.2455	N/A	Monooxygenase	scaffold_10:257174-258091		
F	2	50322	-0.3855	-0.5918	N/A	Hypothetical, Translin-associated protein	scaffold_12:428494-429392		
F	2	190482	-1.1029	-1.3035	N/A	Glycoside hydrolase, family 11	scaffold_13:111536-115689		
F	2	203483	-0.4935	-0.588	N/A	-	scaffold_13:224220-224910		
F	2	191568	-0.5524	-0.7391	N/A	Predicted glutathione S-transferase	scaffold_14:595241-596309		
F	2	54742	-0.6248	-0.7661	N/A	-	scaffold_14:744545-744987		
F	2	135251	-0.558	-0.7705	N/A	Methyltransferase	scaffold_16:177341-178358		
F	2	45530	-1.2108	-1.4282	N/A	GH family 76	scaffold_18:308003-309343		
F	2	126848	-0.6963	-0.9247	N/A	Hypothetical Glucose-6-phosphate/phosphate and phosphoenolpyruvate/phosphate antiporter	scaffold_19:59796-60719		
F	2	52123	-0.4698	-0.5484	N/A	Mitochondrial import inner membrane translocase, subunit TIM23	scaffold_2:358820-359507		
F	2	174185	-0.5285	-0.8437	N/A	-	scaffold_2:3588797-3589528		
F	2	205254	-1.0488	-1.3491	N/A	-	scaffold_21:159025-159657		
F	2	195095	-2.4686	-3.9409	N/A	Related to zink transporter of A. fumigatus	scaffold_21:165794-166864		
F	2	38230	-0.4827	-0.5722	N/A	Acyl-CoA synthetase	scaffold_3:2004643-2006594		
F	2	38285	-0.4692	-0.7067	N/A	Related to Chitin synthase D, Aspergillus fumigatus	scaffold_3:2178151-2180348		
F	2	208150	-0.5326	-0.6215	N/A	FAD-dependent pyridine nucleotide-disulphide oxidoreductase	scaffold_3:2578972-2580902		
F	2	52515	-0.3749	-0.6349	N/A	Predicted thioesterase	scaffold_3:302993-303951		
F	2	177413	-0.5312	-0.7057	N/A	Cytochrome P450	scaffold_3:3306186-3308113		
F	2	48036	-0.4662	-0.637	N/A	-	scaffold_4:1761639-1762706		
F	2	208562	-0.7703	-1.1326	N/A	Hypothetical RNA polymerase II transcription elongation factor Elongin/SIII, subunit elongin C	scaffold_4:243751-244135		
F	2	180093	-0.6988	-0.8507	N/A	-	scaffold_5:1045031-1045861		
F	2	181224	-1.1766	-1.4765	N/A	Oxidosqualene-lanosterol cyclase and related proteins	scaffold_5:1060197-1062714		
F	2	40744	-0.5007	-0.779	N/A	Predicted mitochondrial carrier protein	scaffold_6:1520123-1522327		
F	2	40336	-0.6654	-1.0163	N/A	-	scaffold_6:167442-168188		
F	2	130919	-0.3926	-0.5053	N/A	RING finger protein	scaffold_6:501859-503286		
F	2	211085	-0.3274	-0.4081	N/A	Got1-like protein	scaffold_8:813028-813740		
F	2	186738	-0.5554	-0.8211	N/A	Hypothetical Mg2+ transporter protein, CorA-like. Inner membrane mitochondrial	scaffold_9:389757-391600		
F	2	211517	-2.8771	-3.301	N/A	-	scaffold_9:773838-774629		
F	3	55324	-1.7112	-1.9398	N/A	putative extracellular tyrosinase	scaffold_1:1418913-1420246		
F	3	35857	-1.6826	-1.971	N/A	-	scaffold_1:1576855-1578274		
F	3	170972	-0.9548	-1.2711	N/A	-	scaffold_1:2311734-2312934		
F	3	206273	-0.5343	-0.7244	N/A	Hypothetical MCM3	scaffold_1:3179520-3194377		
F	3	36316	-1.1763	-1.5142	N/A	-	scaffold_1:3239956-3242487		
F	3	36428	-1.6834	-2.544	N/A	-	scaffold_1:3564129-3565487		
F	3	119444	-0.8752	-1.1454	N/A	Hypothetical protein. Possibly a DNA-dependent ATPase (SNF2 related)	scaffold_1:452068-455039		
F	3	172849	-2.0199	-2.3717	N/A	-	scaffold_1:749535-750112		
F	3	35670	-0.8773	-1.2675	N/A	GCN5-related N-acetyltransferase	scaffold_1:995424-995876		
F	3	54080	-0.8147	-1.2505	N/A	-	scaffold_10:161649-163710		
F	3	42784	-1.8853	-2.3681	N/A	-	scaffold_10:703245-705030		
F	3	134470	-0.462	-0.7482	N/A	-	scaffold_11:1153290-1154615		
F	3	188501	-0.6648	-0.8529	N/A	Notchless-like WD40 repeat-containing protein	scaffold_11:1551281-1554572		
F	3	188738	-1.4815	-1.8488	N/A	Hypothetical protein	scaffold_11:1602073-1605411		
F	3	141162	-0.6919	-0.8263	N/A	CRAL/TRIO domain.	scaffold_11:162895-163914		
F	3	43178	-0.6678	-1.0141	N/A	Hypothetical heterokaryon incompatibility factor	scaffold_11:378062-380309		
F	3	50075	-0.3876	-0.52	N/A	DeoxyUTP pyrophosphatase	scaffold_11:430678-431208		
F	3	189633	-0.6409	-1.021	N/A	SNARE protein Syntaxin 1 and related proteins	scaffold_12:344482-345401		
F	3	43711	-1.3293	-1.5984	N/A	β-1,6-N-acetylglucosaminyltransferase	scaffold_12:445477-446652		
F	3	54488	-0.7091	-1.1788	N/A	-	scaffold_12:570503-571564		
F	3	54489	-1.5422	-2.5834	N/A	Hypothetical. Contains aspartic peptidase domain	scaffold_12:578940-579938	14	
F	3	189606	-0.6542	-0.9548	N/A	Fungal specific transcription factor	scaffold_12:583619-584972	14	
F	3	43762	-0.9241	-1.4075	N/A	-	scaffold_12:599390-599991		
F	3	132837	-0.9504	-1.6824	N/A	Fungal transcriptional regulatory protein	scaffold_12:620052-621545		
F	3	43866	-0.8365	-1.2589	N/A	-	scaffold_12:918991-919794		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
F	3	50466	-1.5734	-2.0239	N/A	putative Prolyl 4-hydroxylase, α subunit	scaffold_13:305993-306829		
F	3	54568	-2.6375	-3.2026	N/A	Hypothetical flavin-containing monooxygenase. Located in a putative cluster for secondary metabolism.	scaffold_13:454817-456705		
F	3	54734	-1.4848	-1.8893	N/A	putative extracellular serine carboxypeptidase	scaffold_14:522850-524658		
F	3	191395	-0.6731	-1.0125	N/A	-	scaffold_14:779544-780604		
F	3	50882	-2.4127	-2.9413	N/A	Hypothetical glucose-methanol-choline oxidoreductase (EC 1.99.1.1)	scaffold_15:495081-497129		
F	3	134353	-1.1957	-1.5485	N/A	-	scaffold_15:597744-598849		
F	3	213660	-2.0026	-2.6247	N/A	Leucine rich repeat protein	scaffold_15:73565-75621		
F	3	191829	-1.0031	-1.1922	N/A	Predicted Zn-dependent hydrolase	scaffold_15:800786-801961		
F	3	214109	-0.3619	-0.4371	N/A	UDP-galactose transporter	scaffold_16:856483-857841		
F	3	57332	-0.6242	-0.8125	N/A	Galactosyltransferases	scaffold_17:192996-194399		
F	3	55133	-1.5484	-2.1885	N/A	related to extracellular serine protease	scaffold_19:405679-408073		
F	3	57437	-5.8011	-6.5176	N/A	Hypothetical protein. PFam suggests oxidoreductase activity.	scaffold_19:467860-469127		
F	3	173704	-0.8619	-1.41	N/A	Major facilitator superfamily	scaffold_2:2394402-2396048		
F	3	197679	-1.116	-1.2619	N/A	Amino acid/polyamine transporter	scaffold_2:2739280-2740956		
F	3	174727	-0.6302	-0.9262	N/A	ATP-dependent DNA ligase	scaffold_2:2959968-2961828		
F	3	47166	-0.7814	-0.8809	N/A	-	scaffold_2:3630057-3630937		
F	3	124001	-0.5093	-0.6288	N/A	Postreplication repair protein RAD18	scaffold_20:199329-200484		
F	3	205270	-1.3781	-1.6317	N/A	-	scaffold_21:279394-280182		
F	3	45971	-0.979	-1.4724	N/A	-	scaffold_21:78725-79852		
F	3	55208	-1.7383	-2.1101	N/A	-	scaffold_22:147825-149837		
F	3	195287	-0.993	-1.4444	N/A	-	scaffold_24:66284-67689		
F	3	136048	-0.7655	-1.1072	N/A	Cytochrome c heme-binding site	scaffold_24:99276-100178		
F	3	52590	-1.8439	-2.3526	N/A	putative α-1,3-glucanase, family 71	scaffold_3:1007903-1009297		
F	3	52600	-2.0098	-2.2616	N/A	Glutamate decarboxylase	scaffold_3:1194645-1196347		
F	3	129632	-1.0922	-1.6443	N/A	-	scaffold_3:140405-143435		
F	3	38594	-0.5908	-0.8767	N/A	-	scaffold_3:3362604-3364562		
F	3	52528	-0.9739	-1.2872	N/A	Fungal transcriptional regulatory protein,	scaffold_3:442121-443730		
F	3	52971	-1.8202	-2.3059	N/A	Protein kinase	scaffold_4:1369451-1371078		
F	3	178721	-0.5544	-0.8387	N/A	Hypothetical ATP dependent RNA helicase	scaffold_4:1715127-1717525		
F	3	199424	-1.0799	-1.48	N/A	-	scaffold_4:1790672-1791529		
F	3	56030	-1.845	-2.2185	N/A	Flavin-containing monooxygenase	scaffold_4:2065727-2067565		
F	3	39400	-1.6728	-2.2671	N/A	-	scaffold_4:2401456-2404233		
F	3	38787	-1.7394	-2.3222	N/A	-	scaffold_4:356472-357963		
F	3	179841	-1.4493	-1.7049	N/A	Dynamin	scaffold_4:47467-49875		
F	3	38830	-0.6615	-0.7701	N/A	-	scaffold_4:512243-513838		
F	3	135416	-0.7708	-1.1146	N/A	-	scaffold_4:554650-555634		
F	3	180730	-0.5856	-0.9041	N/A	-	scaffold_5:269937-271016		
F	3	41051	-0.6158	-0.7758	N/A	AMP-dependent synthetase and ligase	scaffold_7:488607-490452		
F	3	185118	-0.422	-0.5165	N/A	Hypothetical N-acetyl transferase, specificity unknown	scaffold_8:774209-774839		
F	3	49515	-0.4269	-0.6091	N/A	-	scaffold_9:227795-229360		
F	3	56689	-0.8666	-1.1738	N/A	-	scaffold_9:802784-804493		
F	4	171338	-1.2248	-1.3178	N/A	Sugar (ANd other) transporter	scaffold_1:1030699-1032478		
F	4	46407	-0.7493	-0.8852	N/A	DEAD/DEAH box helicase	scaffold_1:1053339-1055528		
F	4	205686	-0.7866	-0.9162	N/A	-	scaffold_1:1286005-1287402		
F	4	172733	-0.8603	-0.9486	N/A	Predicted membrane protein	scaffold_1:3862931-3864234		
F	4	187232	-0.9986	-1.014	N/A	-	scaffold_10:146481-148382		
F	4	187731	-1.3506	-1.3652	N/A	-	scaffold_10:608855-614143		
F	4	189922	-2.8102	-2.683	N/A	Cytochrome P450	scaffold_12:561153-562732		
F	4	190177	-0.6706	-0.7563	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae UTP13 gene product; a nucleolar protein, component of the small subunit (SSU) processome containing the U3 snoRNA that is involved in processing of pre-18S rRNA.	scaffold_13:699925-702990		
F	4	191184	-1.0336	-1.1628	N/A	-	scaffold_14:607596-608324		
F	4	45100	-0.7431	-0.7918	N/A	-	scaffold_16:453105-455983		
F	4	45750	-1.3472	-1.3146	N/A	-	scaffold_19:350023-350793		
F	4	125883	-1.2621	-1.496	N/A	-	scaffold_2:2737093-2738364		
F	4	37533	-1.2557	-1.3229	N/A	Unknown. SignalP predicts Anchor	scaffold_2:3632471-3634048		
F	4	214831	-2.279	-2.2116	N/A	HPr serine phosphorylation site	scaffold_21:174465-176774		
F	4	176395	-1.2125	-1.1769	N/A	WD40 repeat-containing protein	scaffold_3:1061073-1062026		
F	4	175980	-0.9193	-0.9373	N/A	Predicted NUDIX hydrolase FGF-2 and related proteins	scaffold_3:2934796-2935661		
F	4	120117	-1.0939	-1.0698	N/A	Fungal transcriptional regulatory protein	scaffold_3:315484-317663		
F	4	178362	-1.1863	-1.1089	N/A	Aromatic-ring hydroxylase	scaffold_4:852414-853971		
F	4	209625	-1.3768	-1.3672	N/A	Generic methyltransferase	scaffold_5:1195615-1196790		
F	4	136009	-0.592	-0.6548	N/A	-	scaffold_5:1300646-1301473		
F	4	53463	-1.546	-1.6586	N/A	Cation efflux family	scaffold_6:1031337-1033131		
F	4	40392	-0.6296	-0.6024	N/A	Hypothetical protein sharing amino acid sequence identity with the Saccharomyces cerevisiae ECM16 gene encoding an essential DEAH-box ATP-dependent RNA helicase specific to the U3 snoRNP; predominantly nucleolar in distribution; required for 18S rRNA synthesis.	scaffold_6:421010-424665		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
F	4	184977	-0.6006	-0.7383	N/A	Hypothetical mitochondrial substrate carrier	scaffold_8:474295-475516		
F	4	49667	-1.2005	-1.1111	N/A	-	scaffold_9:1106312-1108879		
F	4	42341	-1.1153	-1.3929	N/A	-	scaffold_9:948890-950158		
F	5	196241	-1.9299	-1.9872	N/A	-	scaffold_1:1415792-1417121		
F	5	135545	-3.9734	-3.6174	N/A	-	scaffold_1:3203196-3204562		
F	5	172823	-4.1494	-4.3208	N/A	Related to zink transporter of A. fumigatus. Seven putative transmembrane domains and PFam domains for zink transport.	scaffold_1:3457750-3458802		
F	5	36407	-1.8186	-1.3991	N/A	-	scaffold_1:3509217-3509546	15	
F	5	36409	-2.0614	-1.9553	N/A	Ankyrin repeat	scaffold_1:3513617-3517536	15	
F	5	36539	-2.0083	-1.8808	N/A	-	scaffold_1:3874580-3876278		
F	5	35657	-2.1625	-2.0978	N/A	-	scaffold_1:960449-961776		
F	5	140548	-1.9481	-1.7553	N/A	Cytochrome P450	scaffold_10:53187-54784		
F	5	212718	-4.7304	-4.3421	N/A	Hypothetical protein. PFam suggests Oligopeptide transporter activity. 12 transmembrane domains are predicted	scaffold_11:1544965-1547586		
F	5	212729	-2.7559	-2.801	N/A	Short-chain dehydrogenase/reductase	scaffold_11:1560255-1561214		
F	5	43950	-0.9132	-0.7423	N/A	-	scaffold_12:1159690-1160296		
F	5	212915	-3.1496	-2.5265	N/A	hypothetical α-1,3-glucan synthase	scaffold_12:631531-639214		
F	5	43818	-0.4575	-0.3539	N/A	-	scaffold_12:773845-775449		
F	5	44540	-1.2284	-1.121	N/A	Hypothetical. Interpro suggests RmlC-Cupin like domain	scaffold_14:611456-612028		
F	5	57215	-1.3612	-1.2377	N/A	(aphA) extracellular acid phosphatase	scaffold_15:447413-449413		
F	5	191821	-2.6465	-2.5799	N/A	Hypothetical. Predicted transporter (major facilitator superfamily	scaffold_15:635580-637199		
F	5	50918	-1.307	-1.2459	N/A	Putative Major facilitator superfamily, Synaptic vesicle transporter SVOP and related transporters	scaffold_15:767228-768563		
F	5	44948	-2.2889	-2.4867	N/A	-	scaffold_15:931200-933235		
F	5	45730	-5.2762	-5.761	N/A	-	scaffold_19:288657-289241		
F	5	214683	-1.9471	-2.0105	N/A	-	scaffold_19:381076-382329		
F	5	128584	-2.9106	-2.7994	N/A	Non-ribosomal peptide synthetase	scaffold_19:469645-474925		
F	5	175333	-1.9707	-1.7816	N/A	hypothetical K+ potassium transporte	scaffold_2:1416406-1418691		
F	5	197971	-0.871	-0.9031	N/A	-	scaffold_2:3804156-3804866		
F	5	214837	-1.7121	-1.4718	N/A	Hypothetical GABA permease/amino acid permease	scaffold_21:231858-233853		
F	5	55179	-2.0118	-2.077	N/A	-	scaffold_21:29275-29817		
F	5	195111	-1.7116	-1.5105	N/A	General substrate transporter	scaffold_22:86428-88207		
F	5	198296	-2.2408	-2.1262	N/A	-	scaffold_3:1185813-1186802		
F	5	47391	-2.7774	-2.3615	N/A	-	scaffold_3:1474906-1475981		
F	5	52639	-2.5174	-1.9993	N/A	SAM (and some other nucleotide) binding motif	scaffold_3:1800071-1800955		
F	5	38397	-3.6851	-3.3115	N/A	-	scaffold_3:2706239-2706715		
F	5	37733	-2.0966	-1.9445	N/A	-	scaffold_3:271533-272267		
F	5	52517	-2.2776	-2.0109	N/A	Peptidase S10, serine carboxypeptidase	scaffold_3:312065-314895		
F	5	177916	-2.0506	-1.8827	N/A	-	scaffold_3:3439660-3441325		
F	5	52535	-1.196	-1.0552	N/A	-	scaffold_3:489481-490506		
F	5	37942	-0.9645	-0.7613	N/A	Hypothetical Cytochrome P450 monooxygenase	scaffold_3:935574-937104		
F	5	39307	-0.5478	-0.5007	N/A	Major facilitator superfamily	scaffold_4:2098244-2099577		
F	5	39319	-0.3867	-0.3225	N/A	hypothetical protein containing Zn-finger, C2H2 type and G-protein β WD-40 repeat domains	scaffold_4:2135330-2137019		
F	5	179010	-1.777	-1.7717	N/A	-	scaffold_4:2307646-2309089		
F	5	209170	-0.6941	-0.6456	N/A	Hypothetical protein contains SEL1-like repeat	scaffold_4:2859127-2861731		
F	5	179240	-2.594	-2.7838	N/A	hypothetical α-1,6-mannanase. GH family 76	scaffold_4:349960-351741		
F	5	48469	-0.662	-0.6615	N/A	hypothetical lysophospholipase/carboxylesterase family protein	scaffold_5:1618785-1619573		
F	5	180970	-2.0918	-1.9777	N/A	-	scaffold_5:1757877-1758985		
F	5	181710	-1.3929	-1.3835	N/A	Major facilitator superfamily	scaffold_5:2191147-2193271		
F	5	139952	-2.1477	-2.2294	N/A	Cytochrome P450	scaffold_5:2325604-2327380		
F	5	128800	-1.682	-1.7335	N/A	ABC superfamily	scaffold_6:1354623-1358856		
F	5	40820	-0.8373	-0.7285	N/A	Guanine-specific ribonuclease N1 and T1	scaffold_6:1772981-1773501		
F	5	137876	-1.2579	-1.1893	N/A	-	scaffold_6:1802415-1802703		
F	5	181835	-1.986	-2.0893	N/A	-	scaffold_6:1921625-1923230		
F	5	184012	-0.9228	-0.8798	N/A	Amino acid transporters	scaffold_7:153398-154702		
F	5	183352	-2.5504	-2.1767	N/A	Aromatic-ring hydroxylase	scaffold_7:1543026-1544339		
F	5	53699	-2.8861	-2.597	N/A	-	scaffold_7:1569024-1570548		
F	5	41430	-2.7301	-2.3522	N/A	-	scaffold_7:1739591-1740265		
F	5	184267	-1.429	-1.375	N/A	Hypothetical low affinity iron permease	scaffold_7:82038-83474		
F	5	128711	-0.7693	-0.6923	N/A	Helicase, C-terminal	scaffold_8:446892-452576		
F	5	210994	-1.2281	-1.3895	N/A	-	scaffold_8:487246-488631		
F	5	41631	-2.1953	-1.9829	N/A	Amidohydrolase	scaffold_8:541782-543224		
F	5	42198	-3.5685	-3.4914	N/A	-	scaffold_9:529523-530565		
F	6	52031	-5.6468	-5.0269	N/A	O-methyltransferase	scaffold_1:3207123-3208746		
F	6	195867	-2.4273	-2.2436	N/A	-	scaffold_1:68636-69457		
F	6	43466	-1.1326	-1.1062	N/A	-	scaffold_11:1350192-1352044		
F	6	189367	-0.9575	-0.8508	N/A	hypothetical multicopper oxidase with signal peptide motif	scaffold_12:1156266-1158141	16	
F	6	54510	-2.2928	-1.9623	N/A	-	scaffold_12:1162976-1164379	16	
F	6	139271	-2.1553	-1.924	N/A	-	scaffold_14:684080-686360		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
F	6	141096	-3.1703	-2.5749	N/A	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_14:861185-862436		
F	6	133280	-2.4769	-2.2217	N/A	Phosphatidylinositol-specific phospholipase C	scaffold_15:502224-503216		
F	6	44950	-2.7613	-2.7903	N/A	Cytochrome P450	scaffold_15:936061-937751	17	3
F	6	44951	-3.8856	-3.554	N/A	-	scaffold_15:938389-938958	17	3
F	6	44952	-3.6075	-3.5099	N/A	Cytochrome P450	scaffold_15:940917-942014	17	3
F	6	214397	-2.4687	-2.2639	N/A	candidate aminotransferase, classes I and II	scaffold_17:611890-613760		
F	6	214488	-3.4482	-2.8291	N/A	-	scaffold_18:191765-193144		
F	6	143462	-1.8452	-1.7071	N/A	Ankyrin	scaffold_18:566503-566820		
F	6	194162	-3.1742	-3.1751	N/A	Amino acid transporters	scaffold_19:476684-478688		
F	6	46979	-1.6542	-1.4556	N/A	Carboxypeptidase	scaffold_2:1201795-1203621		
F	6	135360	-2.3595	-2.1244	N/A	Lipid phosphate phosphatase and related enzymes of the PAP2 family	scaffold_2:308251-309217		
F	6	52433	-0.9717	-0.9169	N/A	Ankyrin	scaffold_2:3387217-3390818		
F	6	36678	-1.0047	-0.7426	N/A	Nuclear receptor coregulator SMRT/SMRTER, contains Myb-like domains	scaffold_2:350582-351070		
F	6	136287	-1.0839	-1.0107	N/A	Candidate anbA gene,codes for translation initiation factor eIF-5A (in yeast) that promotes formation of the first peptide bond during translation.	scaffold_20:272981-273957		
F	6	45993	-0.7212	-0.5722	N/A	-	scaffold_21:148067-148828		
F	6	55665	-2.7869	-2.3268	N/A	related to tripeptidyl peptidase	scaffold_3:285757-287756		
F	6	38587	-3.0214	-2.7508	N/A	-	scaffold_3:3332240-3334660		
F	6	39906	-2.5627	-2.3652	N/A	-	scaffold_5:1165610-1167226		
F	6	140813	-2.5633	-2.3499	N/A	Hypothetical. Mannosyltransferase ?	scaffold_6:1245114-1246304		
F	6	183931	-1.429	-1.2929	N/A	Hypothetical major drug resistance protein, major facilitator superfamily	scaffold_7:1642537-1644515		
F	6	184876	-1.5863	-1.388	N/A	-	scaffold_8:1576598-1578220		
F	6	53757	-3.0279	-3.0269	N/A	-	scaffold_8:373408-373911		
F	7	43405	-1.6722	-1.3902	N/A	Major facilitator superfamily	scaffold_11:1160142-1161653		
F	7	188620	-3.1349	-2.9809	N/A	Cation transporting ATPase	scaffold_11:1522783-1526109		
F	7	141890	-0.844	-0.8182	N/A	-	scaffold_12:1161208-1162307		
F	7	190297	-1.2407	-1.1951	N/A	-	scaffold_13:174014-174797		
F	7	57126	-0.4611	-0.5335	N/A	-	scaffold_14:36909-38621		
F	7	44909	-0.6799	-0.5592	N/A	Flavin-containing monooxygenase	scaffold_15:816331-818491		
F	7	44989	-1.1853	-0.9052	N/A	-	scaffold_16:111347-112942		
F	7	54860	-0.5494	-0.3934	N/A	purine nucleoside permease	scaffold_16:204743-206027		
F	7	133197	-1.0008	-0.8991	N/A	Transcriptional coactivator	scaffold_18:249574-251124		
F	7	193747	-1.0088	-0.5671	N/A	predicted RNA terminal phosphate cyclase-like protein	scaffold_18:273134-274351		
F	7	194525	-1.1015	-1.034	N/A	Calcium-binding EF-hand	scaffold_19:379849-380696		
F	7	118624	-0.9889	-0.913	N/A	Putative polyketide synthase	scaffold_2:2377785-2389575		
F	7	55198	-0.8362	-0.6378	N/A	Major facilitator superfamily	scaffold_22:26123-27766		
F	7	195305	-0.5418	-0.4744	N/A	Isochorismatase hydrolase	scaffold_24:126124-126690		
F	7	46101	-2.8742	-2.5525	N/A	-	scaffold_24:6832-7668		
F	7	176596	-0.9712	-0.8992	N/A	Cytochrome P450	scaffold_3:1108193-1109838		
F	7	208048	-1.2907	-1.1042	N/A	Nitrate reductase	scaffold_3:2104456-2107409		
F	7	38316	-2.2545	-1.8775	N/A	Non-ribosomal peptide synthetase	scaffold_3:2285713-2289093		
F	7	37734	-1.4713	-1.4318	N/A	-	scaffold_3:276356-278370		
F	7	39076	-1.0378	-0.9107	N/A	-	scaffold_4:1335531-1336964		
F	7	39277	-1.6576	-1.4117	N/A	-	scaffold_4:1994606-1996094		
F	7	181252	-3.0014	-3.1149	N/A	Glycoside hydrolase, family 16	scaffold_5:2200771-2201955		
F	7	40692	-2.4155	-2.128	N/A	Glycosyl hydrolases family 16	scaffold_6:1367240-1369053		
F	7	140217	-1.5883	-1.3938	N/A	Major facilitator superfamily	scaffold_7:102553-104047		
F	7	183669	-0.5981	-0.6223	N/A	Major facilitator superfamily	scaffold_7:4070-5710		
F	7	53620	-1.0817	-0.7668	N/A	related to extracellular phospholipase C	scaffold_7:641456-643148		
F	7	185327	-1.1648	-1.071	N/A	Cation transporting ATPase	scaffold_8:592155-595509		
F	7	211089	-0.377	-0.4032	N/A	Splicing coactivator SRm160/300, subunit SRm300	scaffold_8:817593-819260		
F	7	53994	-3.0591	-2.0755	N/A	-	scaffold_9:982304-983166		
F	8	171018	-0.6534	-0.6717	N/A	-	scaffold_1:1033698-1034672		
F	8	35687	-1.9073	-1.5166	N/A	Hypothetical protein with a 4Fe-4S ferredoxin, iron-sulfur binding domains	scaffold_1:1047789-1048257		
F	8	35727	-0.7133	-0.5304	N/A	-	scaffold_1:1176570-1177514		
F	8	171166	-1.4094	-1.2041	N/A	Major facilitator superfamily	scaffold_1:1391352-1393111		
F	8	171318	-0.7603	-0.4462	N/A	Major facilitator superfamily	scaffold_1:1611954-1613684		
F	8	35925	-1.2575	-0.9408	N/A	HMG-box transcription factor	scaffold_1:1781460-1783088		
F	8	36406	-0.6692	-0.4424	N/A	-	scaffold_1:3506776-3507281		
F	8	50239	-3.2519	-2.6077	N/A	-	scaffold_11:1558276-1558748		
F	8	43953	-1.2378	-1.0631	N/A	-	scaffold_12:1167215-1169258		
F	8	43722	-1.0749	-0.8192	N/A	-	scaffold_12:475705-477261		
F	8	54615	-0.6064	-0.3909	N/A	hypothetical. KOG: von Willebrand factor	scaffold_13:764544-765651		
F	8	193449	-0.7473	-0.5469	N/A	-	scaffold_17:250116-250881		
F	8	214598	-1.1869	-0.8047	N/A	extracellular GH family 28 endo-polygalacturonase A	scaffold_18:570831-571997		
F	8	214686	-2.1106	-2.1107	N/A	-	scaffold_19:383663-385153		
F	8	37199	-0.6987	-0.516	N/A	-	scaffold_2:2499984-2501850		
F	8	175423	-0.6285	-0.5793	N/A	Esterase/lipase/thioesterase	scaffold_2:3422376-3423308		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
F	8	175149	-0.5194	-0.5042	N/A	Splicing coactivator	scaffold_2:3566025-3571955		
F	8	125895	-0.5203	-0.5215	N/A	-	scaffold_2:3824792-3825353		
F	8	118758	-0.8347	-0.6272	N/A	hypothetical protein	scaffold_21:106001-111724		
F	8	46100	-1.4999	-1.5153	N/A	-	scaffold_24:5243-6355		
F	8	207820	-0.7649	-0.619	N/A	Major facilitator superfamily	scaffold_3:1282257-1283997		
F	8	120113	-1.3006	-1.0584	N/A	-	scaffold_3:214512-216680		
F	8	52699	-1.4754	-1.2232	N/A	WD40 repeat	scaffold_3:2271366-2272536		
F	8	37730	-1.8669	-1.7073	N/A	-	scaffold_3:263933-264754		
F	8	177364	-0.4575	-0.3741	N/A	Mitochondrial substrate carrier	scaffold_3:3200525-3201675		
F	8	52587	-0.825	-0.4924	N/A	related to extracellular acid phosphatase	scaffold_3:957711-959218		
F	8	39083	-0.6844	-0.5188	N/A	-	scaffold_4:1365172-1366518		
F	8	39362	-0.6959	-0.4961	N/A	-	scaffold_4:2270143-2270634		
F	8	56033	-0.5089	-0.3489	N/A	prolyl-4-hydroxylase	scaffold_4:2285344-2286855		
F	8	40243	-1.2791	-0.9123	N/A	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_5:2306059-2306904		
F	8	183189	-2.0283	-1.7046	N/A	-	scaffold_7:1372921-1374031		
F	8	49162	-0.4528	-0.3686	N/A	Major facilitator superfamily	scaffold_7:1655481-1657170		
F	8	41754	-1.5003	-1.3647	N/A	-	scaffold_8:901731-904086		
F	8	139819	-0.5176	-0.4189	N/A	-	scaffold_9:1544910-1546659		
F	8	130414	-0.7254	-0.5436	N/A	-	scaffold_9:767438-769648		
F	9	172670	-0.5075	-0.2993	N/A	-	scaffold_1:2966063-2967000		
F	9	211773	-2.1406	-1.7465	N/A	-	scaffold_10:182058-182859		
F	9	43417	-0.7157	-0.6639	N/A	-	scaffold_11:1187867-1189159		
F	9	50467	-1.822	-1.2494	N/A	-	scaffold_13:307802-308925		
F	9	50513	-0.5868	-0.5877	N/A	hypothetical, SAM (and some other nucleotide) binding motif	scaffold_13:552136-553085		
F	9	191413	-0.4902	-0.3848	N/A	Molybdenum cofactor sulfurase	scaffold_14:560872-562353		
F	9	191374	-0.6789	-0.4806	N/A	putative α/β hydrolase	scaffold_14:689800-690804		
F	9	191570	-0.4835	-0.3302	N/A	Major facilitator superfamily	scaffold_14:835117-836944		
F	9	127698	-1.2835	-0.9357	N/A	-	scaffold_16:260443-261011		
F	9	51221	-0.5358	-0.4939	N/A	Hypothetical 3-ketosteroid reductase	scaffold_17:638113-639500		
F	9	55069	-0.6033	-0.3489	N/A	hypothetical GPI anchor protein	scaffold_18:343038-343862		
F	9	55139	-0.945	-1.0509	N/A	-	scaffold_19:437412-439371	18	
F	9	45784	-1.7788	-2.0193	N/A	-	scaffold_19:439856-441031	18	
F	9	120694	-0.6507	-0.413	N/A	candidate Ferric reductase	scaffold_2:3557421-3558623		
F	9	55209	-1.4717	-1.4348	N/A	Isocitrate dehydrogenase, α subunit	scaffold_24:1754-3460	19	
F	9	46099	-2.0785	-1.9264	N/A	-	scaffold_24:3724-4572	19	
F	9	198539	-0.852	-0.8477	N/A	-	scaffold_3:2098994-2102787		
F	9	176127	-1.538	-1.3632	N/A	Predicted hydrolase related to dienelactone hydrolase	scaffold_3:253328-254275		
F	9	176678	-1.0536	-0.9884	N/A	Hypothetical DNA polymerase X	scaffold_3:3022024-3024315		
F	9	47962	-0.9765	-0.6478	N/A	Voltage-gated shaker-like K+ channel, subunit β/KCNAB	scaffold_4:1280490-1281599		
F	9	39155	-0.684	-0.526	N/A	FOG: Ankyrin repeat	scaffold_4:1575971-1576797		
F	9	179332	-0.5762	-0.5337	N/A	Hypothetical protein. Pfam indicate some lipoate-protein ligase B activity, however no sequence similarities were available to support this	scaffold_4:2471794-2472675		
F	9	38793	-0.4613	-0.4238	N/A	-	scaffold_4:375607-376542		
F	9	180715	-0.5352	-0.5334	N/A	hypothetical ubiquitin-dependent hydrolase	scaffold_5:169191-172025		
F	9	200274	-0.4456	-0.478	N/A	TATA-binding protein	scaffold_5:1775501-1776674		
F	9	182424	-0.5742	-0.587	N/A	Myosin class I heavy chain	scaffold_6:1155700-1159895		
F	9	183349	-0.5574	-0.3835	N/A	Cytochrome P450	scaffold_7:51473-53079		
F	9	53611	-0.5258	-0.5239	N/A	-	scaffold_7:568486-570132		
F	9	42087	-0.5768	-0.5031	N/A	-	scaffold_9:189398-190237		
F	9	186614	-0.8413	-0.8182	N/A	-	scaffold_9:621439-622485		
F	10	36360	-1.8317	-1.9914	N/A	CorA-like Mg2+ transporter protein	scaffold_1:3377475-3378624		
F	10	171043	-0.6963	-0.6858	N/A	-	scaffold_1:338088-339017		
F	10	205492	-0.3414	-0.4084	N/A	Protein kinase	scaffold_1:557425-560771		
F	10	46394	-1.707	-1.8887	N/A	hypothetical methionine aminopeptidase	scaffold_1:956321-957985	20	
F	10	35655	-1.7408	-1.8456	N/A	-	scaffold_1:958096-958858	20	
F	10	136205	-0.9101	-1.0958	N/A	-	scaffold_11:1187030-1187662		
F	10	50148	-2.0816	-2.327	N/A	-	scaffold_11:870813-871546		
F	10	50333	-0.9709	-1.3304	N/A	putative extracellular phytase	scaffold_12:506886-508590		
F	10	128862	-0.6355	-0.7159	N/A	ABC transporter	scaffold_14:428514-433091		
F	10	50723	-0.6763	-0.7275	N/A	GAF domain	scaffold_14:487863-489117		
F	10	192375	-1.3736	-1.5266	N/A	DEAD/DEAH box helicase	scaffold_15:69341-71740		
F	10	131913	-0.4956	-0.6565	N/A	Fungal transcriptional regulatory protein	scaffold_15:856067-857365		
F	10	45025	-0.6193	-0.6459	N/A	-	scaffold_16:232184-233325		
F	10	57293	-0.681	-0.6829	N/A	Peptidyl-tRNA hydrolase	scaffold_16:798815-799594		
F	10	45615	-0.6	-0.7013	N/A	-	scaffold_18:601306-602137		
F	10	214735	-0.8333	-1.0637	N/A	Non-ribosomal peptide synthetase	scaffold_19:591315-592161		
F	10	173968	-0.5274	-0.4961	N/A	-	scaffold_2:1970835-1971973		
F	10	173510	-0.869	-1.0284	N/A	Major facilitator superfamily	scaffold_2:3364274-3366295		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
F	10	55185	-1.7022	-1.9721	N/A	-	scaffold_21:151857-153035		
F	10	38006	-1.4535	-1.4894	N/A	Esterase/lipase/thioesterase	scaffold_3:1117922-1118713		
F	10	207846	-1.2004	-1.3855	N/A	putative lipase/esterase (COG0657) with transmembrane domain	scaffold_3:1539677-1540888		
F	10	47754	-0.4666	-0.5267	N/A	-	scaffold_3:3518813-3520205		
F	10	132415	-0.5947	-0.6248	N/A	WD40 protein	scaffold_3:604332-605844		
F	10	208835	-1.0942	-1.2542	N/A	Serine/threonine protein kinase Chk2 and related proteins	scaffold_4:1371618-1372262		
F	10	123216	-2.5256	-2.7898	N/A	FAD linked oxidase, N-terminal	scaffold_4:1942249-1943593		
F	10	39357	-0.8143	-0.9671	N/A	Ankyrin	scaffold_4:2254043-2258214		
F	10	181115	-0.606	-0.6984	N/A	-	scaffold_5:1779525-1782192		
F	10	181510	-0.9909	-1.245	N/A	hypothetical protein with esterase/lipase/thioesterase and signal peptide motifs	scaffold_5:2384335-2385115		
F	10	53191	-1.1059	-1.3053	N/A	-	scaffold_5:555048-556073		
F	10	40588	-1.3199	-1.3831	N/A	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_6:1028724-1029520		
F	10	182498	-0.9892	-1.1287	N/A	Mitochondrial carrier protein	scaffold_6:897965-899132		
F	10	49473	-0.4206	-0.5014	N/A	-	scaffold_8:1646492-1647079		
F	10	56560	-0.9902	-1.1004	N/A	-	scaffold_8:590552-591709		
F	10	42098	-1.2841	-1.4338	N/A	-	scaffold_9:235624-236923		
F	10	49598	-2.7329	-2.8691	N/A	Pyridine nucleotide-disulphide oxidoreductase, class-II	scaffold_9:640040-641098		
F	11	196122	-0.8353	-0.8789	N/A	putative extracellular GH family 16 cell wall glucanse	scaffold_1:1020948-1022015		
F	11	172786	-1.099	-1.0885	N/A	Major facilitator superfamily	scaffold_1:3742942-3744902		
F	11	42809	-0.9302	-1.2279	N/A	Thioredoxin	scaffold_10:778826-779246		
F	11	212334	-0.6371	-0.7187	N/A	Amino acid transporter	scaffold_11:56240-58029		
F	11	213834	-0.3459	-0.3872	N/A	Permease for cytosine/purines	scaffold_15:909580-911324		
F	11	37483	-0.4898	-0.5706	N/A	-	scaffold_2:3492680-3494140		
F	11	174260	-0.6488	-0.7896	N/A	-	scaffold_2:46077-47132		
F	11	55205	-2.0274	-2.2526	N/A	hypothetical short chain dehydrogenase	scaffold_22:118109-119045		
F	11	175596	-1.2421	-1.3191	N/A	-	scaffold_3:132836-133918		
F	11	175896	-0.5836	-0.6564	N/A	Glucose-6-phosphate/phosphate and phosphoenolpyruvate/phosphate antiporter	scaffold_3:309177-310602		
F	11	39106	-0.5416	-0.7014	N/A	-	scaffold_4:1431199-1434012		
F	11	53150	-0.5101	-0.6601	N/A	-	scaffold_5:239311-239970		
F	11	183990	-1.3071	-1.337	N/A	Major facilitator superfamily	scaffold_7:1454028-1455853		
F	11	41367	-0.5817	-0.6821	N/A	Generic methyltransferase	scaffold_7:1550256-1551706		
F	11	53919	-0.9613	-1.0058	N/A	-	scaffold_9:47434-49898		
F	11	42280	-0.7835	-0.9008	N/A	-	scaffold_9:771032-772665		
F	12	172740	-0.5011	-0.5016	N/A	Hypothetical UDP-glucose/GDP-mannose dehydrogenase	scaffold_1:1281738-1283709		
F	12	141555	-2.9042	-1.9583	N/A	candidate iron permease	scaffold_1:1490309-1491391		
F	12	212641	-1.6221	-1.4064	N/A	hypothetical protein with esterase/lipase/thioesterase and signal peptide motifs	scaffold_11:1077954-1080325		
F	12	56871	-0.7427	-0.7477	N/A	Mitochondrial carrier proteins	scaffold_11:74491-75857		
F	12	56930	-1.9121	-1.7288	N/A	Hypothetical sexual differentiation process protein ISP4	scaffold_11:896917-899338		
F	12	54493	-0.8994	-0.8546	N/A	-	scaffold_12:758017-759729		
F	12	45318	-0.5484	-0.4023	N/A	Predicted hydrolase	scaffold_17:233522-234211		
F	12	55566	-0.8324	-0.7473	N/A	Hydroxymethylglutaryl-coenzyme A synthase	scaffold_2:1566731-1568333		
F	12	175986	-0.7872	-0.6537	N/A	-	scaffold_3:1541340-1542203		
F	12	39104	-0.9784	-0.7951	N/A	Metacaspase involved in regulation of apoptosis	scaffold_4:1426762-1428162		
F	12	181047	-0.4715	-0.3648	N/A	Amino acid/polyamine transporter II	scaffold_5:1542542-1544070		
F	12	126001	-1.5029	-0.851	N/A	-	scaffold_7:1545357-1545962		
F	12	41756	-1.8126	-1.6834	N/A	Amidohydrolase	scaffold_8:906568-907830		
F	12	127030	-0.4453	-0.4453	N/A	-	scaffold_9:1380737-1381457		
F	13	196780	-0.6404	-0.499	N/A	Peptidase S26	scaffold_1:3197734-3199486		
F	13	55493	-0.7697	-0.4498	N/A	related to serine protease	scaffold_1:3427902-3430289		
F	13	205564	-0.4267	-0.3922	N/A	candidate. DNA-directed RNA polymerase	scaffold_1:811952-812816		
F	13	42719	-0.3641	-0.2666	N/A	Protein involved in cell cycle control in A. niger	scaffold_10:482656-484020		
F	13	188257	-1.1556	-1.0193	N/A	-	scaffold_11:1462971-1463387		
F	13	50154	-0.5407	-0.3739	N/A	hypothetical ribulose-phosphate 3-epimerase	scaffold_11:911730-912741		
F	13	127268	-0.7622	-0.5875	N/A	-	scaffold_15:504459-505133		
F	13	192370	-2.0172	-1.9308	N/A	-	scaffold_15:915195-915939		
F	13	136740	-1.5033	-1.1859	N/A	-	scaffold_16:450599-451420		
F	13	192625	-0.5392	-0.5658	N/A	-	scaffold_16:474227-475846		
F	13	57366	-0.5082	-0.4054	N/A	-	scaffold_17:583732-584960		
F	13	37136	-0.6848	-0.5332	N/A	hypothetical β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_2:2003118-2004012		
F	13	36666	-2.3875	-2.2249	N/A	Fungal specific transcription factor	scaffold_2:302011-304602	21	
F	13	175292	-2.4695	-2.0527	N/A	-	scaffold_2:306169-307166	21	
F	13	195065	-1.234	-1.0046	N/A	Fatty acid desaturase	scaffold_21:248619-249948		
F	13	55200	-1.417	-1.4011	N/A	-	scaffold_22:46885-49574		
F	13	52507	-0.5775	-0.5178	N/A	-	scaffold_3:157067-158157		
F	13	38327	-1.148	-1.1265	N/A	-	scaffold_3:2326395-2326775		
F	13	132428	-0.8758	-0.8395	N/A	Major facilitator superfamily	scaffold_3:2707193-2708774		
F	13	180792	-1.6965	-1.1136	N/A	Glutathione S-transferase	scaffold_5:1036711-1037406		
F	13	40151	-0.9743	-0.9851	N/A	Caspase-1, p20	scaffold_5:2051363-2054278		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
F	13	180140	-1.317	-1.2792	N/A	-	scaffold_5:997331-997996		
F	13	133626	-0.5776	-0.4701	N/A	Hypothetical DnaJ domain protein	scaffold_6:1686315-1687732		
F	13	40835	-0.6049	-0.4755	N/A	-	scaffold_6:1811037-1812071		
F	13	53696	-1.1796	-0.9073	N/A	Major facilitator superfamily	scaffold_7:1546695-1548669		
F	13	49151	-1.098	-0.7573	N/A	N-acetyltransferase	scaffold_7:1566440-1567495		
F	13	41870	-0.9984	-0.7506	N/A	short chain dehydrogenase	scaffold_8:1261777-1262570		
F	13	53816	-0.4163	-0.3967	N/A	Phospholipid/glycerol acyltransferase	scaffold_8:859154-867254		
F	13	184769	-1.0067	-1.0763	N/A	Cytochrome P450	scaffold_8:985185-986798		
F	13	211589	-0.594	-0.4743	N/A	Candidate tif5 gene encoding translation initiation factor eIF5.	scaffold_9:1120517-1121794		
F	14	35726	-0.4904	-0.3511	N/A	-	scaffold_1:1173095-1174596		
F	14	49811	-0.6724	-0.6334	N/A	DEAD/DEAH box helicase	scaffold_10:395988-398303		
F	14	203168	-0.8325	-0.9005	N/A	-	scaffold_11:1547985-1548835		
F	14	188497	-0.4309	-0.4111	N/A	Fungal specific transcription factor	scaffold_11:480642-483682		
F	14	43663	-1.6697	-1.2562	N/A	-	scaffold_12:274930-277048		
F	14	43745	-0.8637	-0.9031	N/A	-	scaffold_12:557506-558385		
F	14	190964	-0.7045	-0.8135	N/A	Predicted member of the intramitochondrial sorting protein family	scaffold_13:1195181-1195821		
F	14	54540	-0.559	-0.5607	N/A	DAHP synthetase	scaffold_13:294158-295485		
F	14	54832	-0.9668	-0.7555	N/A	Hypothetical Glutathione S-transferase	scaffold_15:629245-630144		
F	14	214000	-0.5731	-0.5762	N/A	-	scaffold_16:586153-587694		
F	14	57431	-0.6637	-0.6242	N/A	Hypothetical CTP synthase	scaffold_19:352037-353938		
F	14	194381	-0.6587	-0.5993	N/A	Putative polyketide synthase	scaffold_19:583914-590870		
F	14	46933	-0.8493	-0.7291	N/A	Sugar (ANd other) transporter	scaffold_2:730990-732831		
F	14	120939	-1.0459	-0.9948	N/A	-	scaffold_21:129394-132269		
F	14	128111	-0.8304	-0.7673	N/A	-	scaffold_3:1037894-1038181		
F	14	55741	-0.4615	-0.3643	N/A	Protein import receptor MAS20	scaffold_3:1698282-1698959		
F	14	55785	-0.3994	-0.4266	N/A	Protein kinase	scaffold_3:2125207-2126427		
F	14	48061	-1.2735	-1.1347	N/A	Hypothetical ABC transporter	scaffold_4:2008346-2013856		
F	14	179916	-0.8594	-0.6744	N/A	-	scaffold_4:2314541-2316169		
F	14	39394	-0.7929	-0.8616	N/A	Transcription factor TFIIS	scaffold_4:2389305-2389818		
F	14	48862	-0.4746	-0.3968	N/A	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae PUS6 and PUS9 gene products; pseudouridine synthase responsible for modification of cytoplasmic and mitochondrial tRNAs.	scaffold_6:1699411-1701033		
F	14	49148	-0.6534	-0.5015	N/A	-	scaffold_7:1530222-1530717		
F	14	41098	-0.8099	-0.6675	N/A	Integral membrane protein	scaffold_7:644635-645594		
F	14	210620	-0.6482	-0.4912	N/A	Predicted protein shares amino acid sequence similarity with the Saccharomyces cerevisiae UTP6 gene product	scaffold_7:715254-716513		
F	14	53918	-0.8661	-0.9471	N/A	Fungal transcriptional regulatory protein	scaffold_9:35776-38131		
F	15	46856	-0.7969	-0.643	N/A	DEAD/DEAH box helicase	scaffold_1:3755725-3757326		
F	15	51780	-0.6431	-0.6159	N/A	Predicted metal-dependent hydrolase of the TIM-barrel fold	scaffold_1:969405-970503		
F	15	42733	-1.2825	-0.6627	N/A	Dihydroxy-acid dehydratase	scaffold_10:533510-535384		
F	15	43756	-1.8191	-1.6794	N/A	-	scaffold_12:580542-581635	22	
F	15	190041	-1.6693	-0.9489	N/A	Bacterial rhodopsin	scaffold_12:582162-583065	22	
F	15	190111	-0.997	-0.9056	N/A	-	scaffold_12:728284-729202		
F	15	190740	-0.5792	-0.4646	N/A	-	scaffold_13:252783-253646		
F	15	44706	-0.516	-0.3327	N/A	-	scaffold_15:169520-170032		
F	15	192136	-0.6647	-0.3808	N/A	Hypothetical protein shares amino acid sequence identity with the Saccharomyces cerevisiae RRS1 gene product; an essential protein that binds ribosomal protein L11 and is required for nuclear export of the 60S pre-ribosomal subunit during ribosome biogenesis	scaffold_15:249543-250290		
F	15	45166	-0.6876	-0.4461	N/A	-	scaffold_16:666443-668078		
F	15	45208	-0.7253	-0.476	N/A	Hypothetical Ribosome biogenesis protein RPF1, contains IMP4 domain	scaffold_16:802597-803928		
F	15	193151	-0.9006	-0.7301	N/A	-	scaffold_17:223583-225013		
F	15	46991	-0.8813	-0.6262	N/A	Peptidase S16, lon protease	scaffold_2:1422011-1425758		
F	15	174264	-0.3967	-0.2881	N/A	-	scaffold_2:3227785-3228558		
F	15	37604	-0.5087	-0.422	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae UTP18 gene product; a possible U3 snoRNP protein involved in maturation of pre-18S rRNA, based on computational analysis of large-scale protein-protein interaction data.	scaffold_2:3871894-3873911		
F	15	173652	-0.4937	-0.3443	N/A	-	scaffold_2:429582-432126		
F	15	206638	-0.4558	-0.3721	N/A	Aconitate hydratase	scaffold_2:841809-844195		
F	15	46951	-0.9754	-0.7749	N/A	Predicted RNA methylase involved in rRNA processing	scaffold_2:893809-895329		
F	15	214825	-2.2814	-1.6371	N/A	Glycosyl transferase, group 1	scaffold_21:119671-128567		
F	15	38107	-0.968	-0.6996	N/A	DEAD/DEAH box helicase	scaffold_3:1587807-1590215		
F	15	127420	-1.0348	-0.6474	N/A	Zn-finger, C2H2 type	scaffold_3:3129947-3130522		
F	15	38568	-0.8087	-0.518	N/A	Fungal transcriptional regulatory protei	scaffold_3:3276103-3277746		
F	15	37798	-1.5745	-0.9586	N/A	-	scaffold_3:459191-459711		
F	15	47267	-0.6835	-0.5884	N/A	Hypothetical. Sequence identity with S.cerevisiae LCP5 gene product involved in maturation of 18S rRNA.	scaffold_3:526038-527204		
F	15	37850	-0.449	-0.3198	N/A	RAN guanine nucleotide release factor	scaffold_3:648201-648935		
F	15	55983	-0.6639	-0.3367	N/A	WD40 repeat protein	scaffold_4:1224235-1226481		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
F	15	52969	-0.6446	-0.5009	N/A	Importin-beta, N-terminal	scaffold_4:1348921-1352488		
F	15	39128	-0.6668	-0.5953	N/A	hypothetical protein related to cytochrome P450 3A7	scaffold_4:1501322-1503045		
F	15	53053	-0.5955	-0.387	N/A	Uroporphyrin III methyltransferase	scaffold_4:2485860-2487524		
F	15	38920	-1.8131	-1.0439	N/A	-	scaffold_4:854613-855489		
F	15	180223	-0.6018	-0.3644	N/A	Mitochondrial substrate carrier	scaffold_5:1823738-1825166		
F	15	56308	-0.5329	-0.426	N/A	ABC transporter	scaffold_6:619123-622574		
F	15	53863	-0.8619	-0.4998	N/A	Ribosomal protein L10	scaffold_8:1202860-1203691		
F	15	41762	-0.9533	-0.6678	N/A	hypothetical RNA helicase	scaffold_8:925446-927479		
G	1	35795	0.5859	0.6482	N/A	Zn-finger, C2H2 type	scaffold_1:1375642-1376818		
G	1	54124	1.5802	1.2159	N/A	Candidate Glutathione S-transferase	scaffold_10:598081-599010		
G	1	43683	5.2796	5.6119	N/A	Hypothetical argininosuccinate synthase (EC 6.3.4.5)	scaffold_12:361405-362649	23	
G	1	190132	5.5292	5.7421	N/A	Iron/ascorbate family oxidoreductases	scaffold_12:364404-365485	23	
G	1	43869	0.4828	0.4237	N/A	Involved in cell cycle control	scaffold_12:924467-925028		
G	1	44533	0.4132	0.6725	N/A	Fungal specific transcription factor (No blast hits!)	scaffold_14:588614-590607		
G	1	192398	0.4387	0.6166	N/A	Hypothetical dihydroorotase (EC 3.5.2.3)	scaffold_15:905836-907332		
G	1	45021	0.6809	0.6912	N/A	pectate lyase A	scaffold_16:223067-224245		
G	1	193670	0.4703	0.5095	N/A	-	scaffold_18:640517-641842		
G	1	173720	0.3274	0.438	N/A	Glucose-methanol-choline oxidoreductase	scaffold_2:2676794-2678516		
G	1	38716	0.4288	0.4225	N/A	Fungal specific transcription factor	scaffold_4:154103-156807		
G	1	53033	1.3703	1.2484	N/A	related to β-1,3-glucanosyltransferase	scaffold_4:2340033-2341820		
G	1	41997	0.6555	0.6888	N/A	-	scaffold_8:1655638-1656315		
G	1	41764	0.6406	0.6477	N/A	-	scaffold_8:931155-931571		
G	1	186504	0.4829	0.7649	N/A	Hypothetical glyceraldehyde 3-phosphate dehydrogenase; EC 1.2.1.12	scaffold_9:686939-688213		
G	2	135398	0.7047	0.6995	N/A	-	scaffold_1:1105785-1106816		
G	2	170262	0.5552	0.4084	N/A	Aldo/keto reductase family proteins	scaffold_1:181250-182428		
G	2	52928	0.4798	0.4196	N/A	EndoInulinase precursor (2,1-beta-D-fructanfructanohydrolase)	scaffold_4:880406-881956		
G	2	185301	0.572	0.4193	N/A	hypothetical carboxylesterase	scaffold_8:241466-243725		
G	3	211774	1.4115	1.0555	N/A	Amino acid/polyamine transporter I	scaffold_10:188151-190318		
G	3	43478	0.9403	0.7829	N/A	-	scaffold_11:1375969-1376965		
G	3	43876	0.7527	0.4535	N/A	Hypothetical. K+-channel ERG and related proteins, contain PAS/PAC sensor domain	scaffold_12:946832-947566		
G	3	45814	0.8505	0.5389	N/A	-	scaffold_19:542338-543833		
G	3	37758	0.5906	0.5133	N/A	hypothetical β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_3:344916-345763		
G	3	38896	0.5158	0.3647	N/A	-	scaffold_4:766666-768126		
G	3	182955	1.1644	1.0291	N/A	-	scaffold_6:1538019-1540076		
G	3	53661	1.2344	0.9543	N/A	-	scaffold_7:1089420-1090439		
G	3	183287	0.4491	0.2727	N/A	Fungal specific transcription factor	scaffold_7:1442408-1444589		
G	3	41821	0.8149	0.5511	N/A	-	scaffold_8:1098246-1099358		
G	3	42206	0.4374	0.327	N/A	-	scaffold_9:567653-568189		
G	4	206342	3.1633	3.6074	N/A	catR, extracellular catalase	scaffold_1:3410339-3412758		
G	4	52059	3.8365	2.8765	N/A	-	scaffold_1:3456321-3456992		
G	4	55227	7.8286	6.2589	N/A	(godA) glucose oxidase precursor	scaffold_1:94021-95838	24	
G	4	205361	3.9621	3.0224	N/A	hypothetical nitrous oxide reductase	scaffold_1:97060-98324	24	
G	4	192362	3.9253	4.1307	N/A	Hypothetical alcohol dehydrogenase	scaffold_15:697442-698524		
G	4	44880	2.7542	2.9053	N/A	Non-ribosomal peptide synthetase	scaffold_15:727042-731289		
G	4	123301	0.5312	0.3393	N/A	Amino acid/polyamine transporter	scaffold_20:13951-15185		
G	4	51482	1.5394	0.9397	N/A	Major facilitator superfamily	scaffold_21:195252-196959		
G	4	48790	0.8115	0.5976	N/A	Major facilitator superfamily	scaffold_6:1327019-1328539		
G	4	40895	1.2204	0.6809	N/A	von Willebrand factor and related coagulation proteins	scaffold_6:2020675-2023308		
G	4	127791	3.147	2.8967	N/A	putative extracellular protein	scaffold_7:1664166-1664652		
H	1	206090	-0.713	N/A	-0.566	Predicted P-loop ATPase	scaffold_1:2536388-2539683		
H	1	202811	-0.378	N/A	-0.3527	Molecular chaperone (HSP90 family)	scaffold_11:138879-141087		
H	1	134207	-0.5329	N/A	-0.6919	Predicted DNA-dependent RNA polymerase I	scaffold_12:154619-155716		
H	1	132324	-0.7219	N/A	-0.5617	Predicted seven transmembrane receptor - rhodopsin family	scaffold_16:480168-481896		
H	1	192466	-0.442	N/A	-0.5883	-	scaffold_16:576340-578755		
H	1	51257	-0.6796	N/A	-0.5753	Deduced translation product shares amino acid sequence identity with the Saccharomyces cerevisiae NOP14 gene product; a aucleolar protein that forms a complex with Noc4p and mediates maturation and nuclear export of 40S ribosomal subunits; also present in the small subunit processome complex, which is required for processing of pre-18S rRNA.	scaffold_18:116089-118911		
H	1	141670	-0.4061	N/A	-0.4273	-	scaffold_19:355133-356315		
H	1	194752	-0.7963	N/A	-0.8882	-	scaffold_20:47110-49883		
H	1	45989	-1.7232	N/A	-1.106	hypothetical UDP-glucose 4-epimerase	scaffold_21:133983-135293		
H	1	52919	-0.6763	N/A	-0.6415	Hypothetical. Intrpro: AMP-dependent synthetase and ligase	scaffold_4:798919-800973		
H	1	53273	-0.3831	N/A	-0.4397	Protein kinase	scaffold_5:1326848-1328601		
H	1	180480	-0.3872	N/A	-0.4134	-	scaffold_5:2417948-2419288		
H	1	210766	-1.065	N/A	-1.4697	-	scaffold_7:1480130-1482172		
H	1	211648	-0.4747	N/A	-0.4439	ATP-dependent RNA helicase	scaffold_9:1317002-1318903		
H	2	190170	-0.7586	N/A	-0.6834	Major facilitator superfamily	scaffold_12:725657-727177		
H	2	54836	-1.0545	N/A	-0.7889	Fungal transcriptional regulatory protein	scaffold_15:724128-726426		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
H	2	54900	-0.5031	N/A	-0.5102	Predicted GTP-binding protein MMR1	scaffold_16:588169-590163		
H	2	38160	-0.4679	N/A	-0.5173	Hypothetical. Some identity with Nuclear Assembly Factor	scaffold_3:1773469-1775472		
H	2	181371	-0.6407	N/A	-0.51	Molecular chaperones HSP70	scaffold_5:90569-92386		
H	2	46226	-0.4706	N/A	-0.6576	Splicing coactivator SRm160/300, subunit SRm300	scaffold_824:450-1137		
H	2	211661	-1.1798	N/A	-1.0256	Candidate malic oxidoreductase (EC 1.1.1.40)	scaffold_9:1396055-1398425		
H	3	205459	-0.506	N/A	-0.3881	Alpha-isopropylmalate synthase/homocitrate synthase	scaffold_1:491217-493367		
H	3	44776	-0.8145	N/A	-0.5548	-	scaffold_15:396331-399873		
H	3	50921	-0.6777	N/A	-0.3978	hypothetical Short-chain dehydrogenase/reductase SDR	scaffold_15:823195-824193		
H	3	54890	-0.7541	N/A	-0.4684	Carbamoyl-phosphate synthase	scaffold_16:512538-513899		
H	3	132154	-1.0455	N/A	-0.6563	Cytochrome P450	scaffold_2:96080-97785		
H	3	195119	-0.6646	N/A	-0.4778	Esterase/lipase/thioesterase	scaffold_22:72840-73472		
H	3	37662	-0.4803	N/A	-0.3381	Cytochrome P450	scaffold_3:27827-28620		
H	3	176830	-0.8248	N/A	-0.563	WD40 repeat nucleolar protein putatively involved in ribosome biogenesis	scaffold_3:3456924-3459290		
H	3	183936	-0.6789	N/A	-0.4503	Related to deoxyhypusine synthase.	scaffold_7:1489497-1490702		
H	3	41761	-0.6163	N/A	-0.4737	Predicted RNA-binding protein	scaffold_8:922729-924861		
H	4	46410	-0.7241	N/A	-0.4825	Predicted protein involved in nuclear export of pre-ribosomes	scaffold_1:1063208-1065580		
H	4	206020	-0.7322	N/A	-0.5249	Hypothetical. involved in rRNA processing. associates with trans-acting ribosome biogenesis factors (yeast); similar to β-transducin superfamily.	scaffold_1:2302260-2303964		
H	4	36405	-0.3928	N/A	-0.288	-	scaffold_1:3506061-3506495		
H	4	190162	-1.5313	N/A	-1.0493	Amino acid transporters	scaffold_12:990502-992299		
H	4	54864	-0.5593	N/A	-0.4877	Aromatic-ring hydroxylase	scaffold_16:263009-264486		
H	4	51246	-0.5708	N/A	-0.4287	Hypothetical glucose-methanol-choline oxidoreductase (EC 1.99.1.1)	scaffold_18:71102-72833		
H	4	46903	-0.7989	N/A	-0.4941	WD40-repeat-containing subunit of the 18S rRNA processing complex	scaffold_2:432575-434176		
H	4	176418	-0.4741	N/A	-0.3286	-	scaffold_3:1732685-1733381		
H	4	38286	-0.8137	N/A	-0.4427	FOG: RRM domain	scaffold_3:2182852-2184124		
H	4	52754	-1.1141	N/A	-0.7408	Nucleolar protein NOP52/RRP1	scaffold_3:2840184-2841271		
H	4	208547	-0.9746	N/A	-0.6008	ATP-citrate lyase	scaffold_4:185013-187200		
H	4	180337	-0.7614	N/A	-0.6709	Hypothetical. KOG suggests transcription regulation/DEAD box	scaffold_5:957990-958754		
H	4	210454	-0.6363	N/A	-0.3611	Molecular chaperones mortalin/PBP74/GRP75, HSP70 superfamily	scaffold_7:310817-313072		
I	1	35976	0.7982	N/A	0.8439	Major facilitator superfamily	scaffold_1:1926846-1928620		
I	1	131120	0.6104	N/A	0.559	AAA ATPase	scaffold_1:2180249-2182052		
I	1	55399	1.1781	N/A	1.3597	Predicted α/β hydrolase	scaffold_1:2240060-2241273		
I	1	170303	0.3665	N/A	0.3572	Cytochrome P450	scaffold_1:827835-829740		
I	1	211815	1.9347	N/A	1.437	Hypothetical. Interpro suggests Nitrilase/cyanide hydratase and apolipoprotein N-acyltransferase	scaffold_10:343392-344506		
I	1	134478	0.4416	N/A	0.3597	-	scaffold_10:381338-382613		
I	1	189793	0.8884	N/A	0.8962	-	scaffold_12:86153-86929		
I	1	191350	2.5001	N/A	1.9021	-	scaffold_14:103714-105193		
I	1	50817	0.6039	N/A	0.5462	Hypothetical hexokinase; EC 2.7.1.1; phosphorylation of glucose and fructose	scaffold_15:138487-140136		
I	1	44758	1.6584	N/A	1.5497	Predicted transporter	scaffold_15:328226-330161		
I	1	47045	0.3595	N/A	0.3884	-	scaffold_2:1957804-1958547		
I	1	37191	0.4279	N/A	0.353	Amidase	scaffold_2:2471142-2472096		
I	1	173803	0.7767	N/A	0.6962	-	scaffold_2:3549859-3550824		
I	1	45908	0.743	N/A	0.8605	-	scaffold_20:225052-225804		
I	1	214849	1.208	N/A	1.1935	FAD-dependent pyridine nucleotide-disulphide oxidoreductase	scaffold_22:20345-22316		
I	1	176050	2.4669	N/A	1.8635	Surface binding protein	scaffold_3:1063382-1063960		
I	1	55742	1.0052	N/A	0.5923	aldA Aldehyde dehydrogenase (aldA) (EC 1.2.1.3)	scaffold_3:1716050-1717722		
I	1	177292	0.5148	N/A	0.3753	-	scaffold_3:188326-189579		
I	1	175987	0.9357	N/A	0.8862	Carbon-nitrogen hydrolase	scaffold_3:195555-196683		
I	1	177736	1.6446	N/A	1.3805	hypothetical short chain dehydrogenase	scaffold_3:3168548-3169513		
I	1	118629	0.7996	N/A	0.7703	Hypothetical polyketide synthase	scaffold_4:2490985-2498440		
I	1	52870	2.4753	N/A	2.1263	Sugar (ANd other) transporter	scaffold_4:322912-324749		
I	1	199148	0.5399	N/A	0.5525	Candidate Fumarylacetoacetase	scaffold_4:576251-577546		
I	1	38912	1.237	N/A	1.3433	Hypothetical amidase (EC 3.5.1.4)	scaffold_4:830538-832517		
I	1	121695	1.6861	N/A	1.7517	AMP-dependent synthetase and ligase	scaffold_5:1245847-1247716		
I	1	182246	1.4861	N/A	1.4783	-	scaffold_6:1002946-1004025	25	
I	1	133925	0.6963	N/A	0.6986	Peptidase M12B	scaffold_6:1006493-1007524	25	
I	1	210373	1.5528	N/A	1.4849	Cyanate lyase	scaffold_6:1799553-1800154		
I	1	48680	2.111	N/A	2.1809	Malate synthase	scaffold_6:605531-607330		
I	1	200605	1.576	N/A	1.3412	(abfB) α-L-arabinofuranosidase B	scaffold_6:710307-711806		
I	1	53663	1.5777	N/A	1.3401	-	scaffold_7:1157628-1158919	26	
I	1	41259	1.5546	N/A	1.4815	Protein kinase	scaffold_7:1163296-1164297	26	
I	1	183509	0.8674	N/A	0.6674	-	scaffold_7:1422001-1422833		
I	1	49135	2.0893	N/A	1.9731	Gamma-butyrobetaine,2-oxoglutarate dioxygenase	scaffold_7:1448866-1450405	27	
I	1	183506	1.8437	N/A	1.6038	sugar transporter	scaffold_7:1451543-1453107	27	
I	1	136826	0.8676	N/A	0.6744	Short-chain dehydrogenase/reductase SDR	scaffold_7:1588027-1588837		
I	1	53657	0.5292	N/A	0.4795	Tyrosine protein kinase	scaffold_7:963894-966229		
I	1	53658	1.3126	N/A	1.026	-	scaffold_7:974963-975730		
I	1	195767	1.1182	N/A	0.9614	-	scaffold_780:2-322		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
I	1	210988	1.1969	N/A	1.1532	candidate cell wall protein	scaffold_8:466699-467316		
I	1	184679	0.924	N/A	0.746	Calcium/proton exchanger superfamily	scaffold_8:518773-521058		
I	1	41666	1.0954	N/A	1.1116	-	scaffold_8:637199-637573		
I	1	53793	0.8203	N/A	0.9223	-	scaffold_8:655520-657107		
I	1	54016	0.6413	N/A	0.6613	Hypothetical high-affinity nickel transport protein	scaffold_9:1182140-1183908		
I	1	56739	2.1589	N/A	1.8587	Ornithine-N5-oxygenase	scaffold_9:1600084-1601640		
I	2	170414	0.8816	N/A	0.5811	short chain dehydrogenase	scaffold_1:1341845-1342726		
I	2	196237	5.616	N/A	4.7467	(acuD) Isocitrate lyase	scaffold_1:1408184-1410033		
I	2	127436	1.7895	N/A	1.3286	Carbohydrate kinase	scaffold_1:1894348-1895182		
I	2	44111	0.8007	N/A	0.6521	-	scaffold_13:429455-431536		
I	2	213185	0.9847	N/A	0.6807	Pyruvate carboxylase (EC 6.4.1.1)	scaffold_13:641148-644786		
I	2	50844	0.9396	N/A	0.7205	Hypothetical Fungal specific transcription factor	scaffold_15:223761-226602		
I	2	213779	2.089	N/A	1.7955	-	scaffold_15:459021-460049		
I	2	204276	5.7217	N/A	3.2702	Zinc-containing alcohol dehydrogenase	scaffold_15:917460-918725		
I	2	204333	2.7375	N/A	2.2734	DUF1275 domain protein	scaffold_16:215477-216354		
I	2	193984	1.6443	N/A	1.5726	C4-dicarboxylate transporter/malic acid transport protein	scaffold_18:254282-255529		
I	2	214587	3.6601	N/A	2.6286	Acetyl-CoA hydrolase	scaffold_18:551749-553494		
I	2	45804	1.3632	N/A	1.0359	hypothetical extracellular FAD/FMN-containing dehydrogenase	scaffold_19:510107-511715		
I	2	174968	0.5471	N/A	0.5258	-	scaffold_2:3268601-3269989		
I	2	142689	0.8427	N/A	0.6725	-	scaffold_21:190826-191565	28	
I	2	55188	1.9461	N/A	1.9548	DP87 protein (prespore protein in Dichostelium)	scaffold_21:192901-193884	28	
I	2	133851	0.5743	N/A	0.4683	-	scaffold_4:2295404-2297108		
I	2	180549	2.8069	N/A	2.479	-	scaffold_5:1169607-1170368		
I	2	180604	0.4745	N/A	0.2921	Hydantoinase/oxoprolinase	scaffold_5:2345628-2348930		
I	2	142331	2.3151	N/A	1.8617	Short-chain dehydrogenase/reductase SDR	scaffold_6:1004458-1005475		
I	2	182538	0.6632	N/A	0.4189	-	scaffold_6:550050-553217		
I	2	41246	0.6913	N/A	0.4024	Fungal transcriptional regulatory protein, N-terminal	scaffold_7:1123992-1126398		
I	2	41379	1.529	N/A	1.2115	Fungal transcriptional regulatory protein, N-terminal	scaffold_7:1582910-1584704		
I	2	132538	1.6046	N/A	1.2754	Sorbin and SH3 domain-containing protein (signal transduction)	scaffold_7:224933-226638		
I	2	41014	0.6152	N/A	0.4275	Oxidoreductase family	scaffold_7:385056-386189		
I	2	41820	1.2118	N/A	0.9245	-	scaffold_8:1097283-1097972		
I	2	184563	0.518	N/A	0.403	-	scaffold_8:1331478-1331735		
I	2	184760	2.3634	N/A	2.0132	-	scaffold_8:1363233-1364592		
I	2	210891	0.3467	N/A	0.2495	Amidase	scaffold_8:195834-197828		
I	3	122511	0.7619	N/A	0.8359	Major facilitator superfamily	scaffold_1:2256048-2257686		
I	3	170148	1.2653	N/A	1.3837	putative GH family 18 endo-chitinase	scaffold_1:2343979-2344971		
I	3	172302	3.6793	N/A	4.0369	Hypothetical Coenzyme A transferase	scaffold_1:3898421-3900575		
I	3	212549	1.1216	N/A	1.1451	-	scaffold_11:738872-740389		
I	3	190222	0.7528	N/A	0.6746	-	scaffold_13:519551-520777		
I	3	44000	1.459	N/A	1.3913	hypothetical Isochorismatase hydrolase	scaffold_13:88565-89214		
I	3	119606	0.7577	N/A	0.7209	Trehalose-6-phosphate synthase component TPS1 and related subunits	scaffold_15:112042-114765		
I	3	192500	0.661	N/A	0.5433	Fungal transcriptional regulatory protein	scaffold_16:507449-509197		
I	3	193097	0.753	N/A	0.6297	Major facilitator superfamily	scaffold_16:570674-572509		
I	3	120801	2.062	N/A	1.8698	Fungal specific transcription factor	scaffold_18:613273-615247	29	
I	3	193657	6.1482	N/A	4.601	Monocarboxylate transporter	scaffold_18:615404-616985	29	
I	3	173536	1.0581	N/A	0.9345	Glutathione S-transferase	scaffold_2:3285358-3286056		
I	3	132141	1.1464	N/A	1.016	AMP-dependent synthetase and ligase	scaffold_3:1692761-1694521		
I	3	52774	1.8595	N/A	1.6602	Hypothetical non-ribosomal peptide synthetase	scaffold_3:3065698-3085018		
I	3	38745	1.6582	N/A	1.5524	Glycosyl transferase, family 28	scaffold_4:224345-227250		
I	3	40468	0.9937	N/A	0.8169	Aromatic-ring hydroxylase	scaffold_6:655733-656995		
I	3	56474	0.6563	N/A	0.7008	-	scaffold_7:1175096-1176560		
I	3	131431	1.1794	N/A	0.8847	Hypothetical. Flavoprotein monooxygenase domain	scaffold_7:1686955-1688349		
I	3	56390	0.8035	N/A	0.7981	related to aspartate transaminase D-chain S. cerevisiae	scaffold_7:221755-223355		
I	3	49063	2.0854	N/A	2.2521	Hypothetical fatty acid omega-hydroxylase	scaffold_7:847894-851545		
I	3	41216	0.6602	N/A	0.5612	-	scaffold_7:983817-985157		
I	3	184541	1.1635	N/A	0.904	-	scaffold_8:652739-653733		
I	3	42534	0.9814	N/A	0.7467	-	scaffold_9:1570984-1572261		
I	3	49535	0.8568	N/A	0.8243	FMN-dependent α-hydroxy acid dehydrogenase	scaffold_9:326587-327991		
I	3	42290	1.2731	N/A	1.3625	-	scaffold_9:798083-798755		
I	4	196458	1.8656	N/A	1.4566	-	scaffold_1:2116704-2117675		
I	4	36048	1.3491	N/A	1.0205	-	scaffold_1:2132868-2133558		
I	4	51951	1.295	N/A	1.0002	hypothetical cell wall bound protein/C-type lectin	scaffold_1:2374698-2375490		
I	4	206266	1.157	N/A	0.9411	Cytochrome P450	scaffold_1:3172767-3174571		
I	4	123517	0.8817	N/A	0.6143	short chain dehydrogenase	scaffold_10:1192472-1193593		
I	4	42981	0.7534	N/A	0.4421	Lanthionine synthetase C-like protein	scaffold_10:1751206-1753013		
I	4	187066	0.2891	N/A	0.2542	Glucose/ribitol dehydrogenase	scaffold_10:286086-286554		
I	4	187950	0.7376	N/A	0.4548	Protein kinase	scaffold_10:313889-315349		
I	4	42679	2.1071	N/A	1.9338	Glucose/ribitol dehydrogenase	scaffold_10:345316-346426		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
I	4	140623	1.2952	N/A	1.0825	Cytochrome P450	scaffold_10:586514-587941		
I	4	212946	0.9352	N/A	0.7113	ABC transporter	scaffold_12:1027464-1032019		
I	4	50757	4.6555	N/A	4.376	-	scaffold_14:745771-747605		
I	4	192976	0.805	N/A	0.7738	Iron/ascorbate family oxidoreductases	scaffold_16:219904-221266		
I	4	55072	0.9605	N/A	0.732	Fungal transcriptional regulatory protein	scaffold_18:357292-358860		
I	4	214662	1.7534	N/A	1.2624	hypothetical transporter	scaffold_19:274060-275630		
I	4	214667	1.0087	N/A	0.884	Hypothetical Xanthine dehydrogenase	scaffold_19:319107-323523		
I	4	45823	0.6109	N/A	0.5924	Fungal specific transcription factor	scaffold_19:569238-572488		
I	4	214738	0.6931	N/A	0.5403	Iron/ascorbate family oxidoreductases	scaffold_19:593113-594191		
I	4	36573	2.4189	N/A	1.9048	-	scaffold_2:10478-11232		
I	4	206434	3.0119	N/A	2.1296	Related to glucose transporter	scaffold_2:195523-197341		
I	4	119202	0.471	N/A	0.2671	Ubiquitin-conjugating enzymes	scaffold_2:2587953-2591271		
I	4	207264	1.4702	N/A	1.283	Glycoside hydrolase, family 27	scaffold_2:3135238-3136983		
I	4	47124	2.1854	N/A	1.9382	-	scaffold_2:3169347-3170746		
I	4	173284	1.2303	N/A	0.9811	-	scaffold_2:3590991-3592238		
I	4	52126	1.7078	N/A	1.0934	Hypothetical endoglucanase	scaffold_2:412976-413425		
I	4	174873	0.4547	N/A	0.4272	Hypothetical N-acetyltransferase according to PFam. No supporting sequence information	scaffold_2:913840-914773		
I	4	122978	2.3348	N/A	1.9271	hypothetical extracellular GH family 43 β-gaclatosidase, exo-beta-1,3-galactanase	scaffold_3:202072-203885		
I	4	208648	0.4156	N/A	0.3524	Hypothetical ABC transporter	scaffold_4:560271-565379		
I	4	134257	0.7417	N/A	0.515	-	scaffold_5:2091925-2093016		
I	4	56172	1.3888	N/A	1.3555	putative GH family 16 GPI-glucanosyltransferase	scaffold_5:750036-751437		
I	4	39594	0.5343	N/A	0.453	SPRT-like metalloprotease	scaffold_5:96897-98114		
I	4	210217	1.5606	N/A	1.2223	large β-ketoacyl synthase probably involved in polyketide synthesis (aurasperone??)	scaffold_6:1083010-1091184	30	4
I	4	210220	1.627	N/A	1.2131	Short-chain dehydrogenase/reductase SDR	scaffold_6:1091638-1092690	30	4
I	4	40885	1.7259	N/A	1.2968	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_6:1981876-1982791		
I	4	181979	1.3542	N/A	1.0864	related to isoamyl alcohol oxidase	scaffold_6:629041-630939		
I	4	51633	1.1298	N/A	1.0998	(bioA) Biotin synthase	scaffold_6:644468-645703		
I	4	120556	0.7962	N/A	0.5161	Helicase-like transcription factor HLTF/DNA helicase RAD5	scaffold_7:1185714-1187823		
I	4	201205	3.9458	N/A	3.48	Hypothetical, putative BYS1 domain	scaffold_7:1386729-1387208		
I	4	53801	2.1188	N/A	1.6544	Hypothetical protein. HMMPfam indicates Glucose-methanol-choline oxidoreductase activity	scaffold_8:739586-741418		
I	4	53802	0.8454	N/A	0.7188	-	scaffold_8:757580-757954		
I	4	53978	2.4372	N/A	1.6667	(mstA) high affinity monosaccharide transporter	scaffold_9:500241-502063		
I	5	206038	1.0484	N/A	0.6094	-	scaffold_1:2349882-2350704		
I	5	119939	0.6536	N/A	0.4255	Fungal specific transcription factor	scaffold_1:3526608-3528627		
I	5	51753	0.7992	N/A	0.7439	-	scaffold_1:682941-683837		
I	5	43481	0.6543	N/A	0.635	-	scaffold_11:1386341-1387290		
I	5	202949	1.0033	N/A	0.7966	Hypothetical. Has similarity to β-1,6-N-acetylglucosaminyltransferase (KOG), contains WSC domain	scaffold_11:494883-496094		
I	5	54375	0.5803	N/A	0.5555	catalase	scaffold_11:991295-993652		
I	5	43781	1.2381	N/A	1.1372	-	scaffold_12:648337-649374		
I	5	43875	0.6894	N/A	0.6269	Aminotransferase, class IV	scaffold_12:942427-943706		
I	5	44401	1.031	N/A	0.8689	-	scaffold_14:142435-143530		
I	5	213685	0.7357	N/A	0.7517	-	scaffold_15:126404-128434		
I	5	45610	0.6686	N/A	0.6907	Sugar (ANd other) transporter	scaffold_18:576246-578108		
I	5	214467	1.2584	N/A	1.2416	Major facilitator superfamily	scaffold_18:98202-100046		
I	5	45821	0.7461	N/A	0.5891	(pelB) extracellular pectin lyase B	scaffold_19:562529-563900		
I	5	173247	2.3886	N/A	1.8451	Candidate phosphate transporter	scaffold_2:103617-105578		
I	5	36954	1.2275	N/A	0.999	-	scaffold_2:1373844-1375062		
I	5	37029	1.658	N/A	1.5864	Ferric reductase like transmembrane component	scaffold_2:1637091-1639038		
I	5	135230	0.8742	N/A	0.589	-	scaffold_2:2562223-2563375		
I	5	206509	0.6853	N/A	0.759	-	scaffold_2:490478-492418		
I	5	55164	1.9343	N/A	1.4204	-	scaffold_20:158570-160008		
I	5	214820	1.2684	N/A	1.0571	Oxidoreductase, N-terminal	scaffold_21:86353-87640		
I	5	55775	0.5007	N/A	0.5934	Guanine nucleotide binding protein (G-protein)	scaffold_3:2069615-2071017		
I	5	38332	1.0391	N/A	0.6862	-	scaffold_3:2338964-2340236		
I	5	52722	0.6348	N/A	0.6112	Predicted membrane protein	scaffold_3:2611882-2613933		
I	5	47585	0.7406	N/A	0.786	Hypothetical pentafunctional AROM protein	scaffold_3:2668851-2671670	31	
I	5	47586	0.7302	N/A	0.7975	Fungal specific transcription factor	scaffold_3:2673461-2676088	31	
I	5	38983	0.7038	N/A	0.5705	Nucleolar GTPase/ATPase p130	scaffold_4:1033309-1038170		
I	5	178503	0.3541	N/A	0.303	Fungal transcriptional regulatory protein	scaffold_4:1134372-1135991		
I	5	56031	1.1163	N/A	0.9331	Fungal transcriptional regulatory protein	scaffold_4:2179054-2182013		
I	5	178365	1.6161	N/A	1.7022	hypothetical aspartic protea	scaffold_4:2299358-2300713		
I	5	38758	0.5203	N/A	0.4996	Fungal specific transcription factor	scaffold_4:258311-260517		
I	5	131149	0.954	N/A	0.721	-	scaffold_5:1434169-1436204		
I	5	139037	0.733	N/A	0.6569	hypothetical β-glucosidase	scaffold_5:724862-727440		
I	5	210233	1.323	N/A	1.0477	-	scaffold_6:1183078-1183898		
I	5	48811	1.3913	N/A	1.3969	(xlnR) Transcriptional activator xlnR	scaffold_6:1466599-1469344		
I	5	126469	0.8121	N/A	0.5673	Heat shock transcription factor	scaffold_7:1001499-1002592		
I	5	41163	0.6622	N/A	0.6879	unknown (decarboxylase ?)	scaffold_7:838808-839609		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
I	5	46166	0.768	N/A	0.6209	Cytochrome P450	scaffold_71:7124-7933		
I	5	49482	0.5824	N/A	0.4918	Amino acid/polyamine transporter II	scaffold_8:1700820-1702737	32	
I	5	184568	0.5816	N/A	0.581	-	scaffold_8:1704172-1705092	32	
I	5	56643	1.2337	N/A	1.2968	Major facilitator superfamily	scaffold_9:103460-105439		
I	6	205766	2.9826	N/A	3.3183	Sugar (ANd other) transporter	scaffold_1:1541708-1543543		
I	6	55270	1.1136	N/A	1.521	-	scaffold_1:676927-679801		
I	6	212167	0.583	N/A	0.5333	Zinc-containing alcohol dehydrogenase superfamily	scaffold_10:1723259-1726075		
I	6	137474	1.0592	N/A	0.9307	-	scaffold_10:1901190-1901850		
I	6	56923	1.0295	N/A	1.2431	-	scaffold_11:790374-793451		
I	6	43664	1.1743	N/A	1.2216	Esterase/lipase/thioesterase	scaffold_12:281584-283779		
I	6	126948	0.7297	N/A	0.8195	-	scaffold_16:77607-78298		
I	6	125201	0.6192	N/A	0.6303	Esterase/lipase/thioesterase	scaffold_2:2985352-2986403		
I	6	176911	0.4067	N/A	0.4149	-	scaffold_3:1962859-1965612		
I	6	138876	1.6139	N/A	1.5556	β-mannosidase A	scaffold_4:1690053-1693070		
I	6	48063	0.4312	N/A	0.6574	Predicted starch-binding protein	scaffold_4:2049197-2050343		
I	6	179936	1.0693	N/A	0.9905	-	scaffold_4:919167-919969		
I	6	180885	0.6128	N/A	0.6038	Fungal transcriptional regulatory protein	scaffold_5:2148224-2151260		
I	6	40476	2.9355	N/A	2.839	-	scaffold_6:682453-683936		
I	6	210182	0.8091	N/A	0.8704	-	scaffold_6:889774-892641		
I	6	53845	0.6395	N/A	0.7748	-	scaffold_8:1094346-1094903		
I	6	137517	0.4257	N/A	0.4716	Cutinase	scaffold_8:564816-565666		
I	6	42186	1.3572	N/A	1.1834	-	scaffold_9:496604-497287		
I	7	46465	0.5836	N/A	0.7072	Taurine catabolism dioxygenase	scaffold_1:1336804-1338104		
I	7	170709	0.8873	N/A	1.1874	Aldehyde dehydrogenase	scaffold_1:1642434-1644196		
I	7	51895	1.4098	N/A	1.8371	Candidate C14-sterol reductase, ergosterol biosynthesis protein	scaffold_1:1959066-1960657		
I	7	170260	0.7817	N/A	0.6794	-	scaffold_1:2337004-2339406		
I	7	36424	1.3279	N/A	1.5992	phosphoglycerate mutase	scaffold_1:3555328-3555963		
I	7	195962	0.881	N/A	1.227	Amino acid transporters	scaffold_1:449825-451605		
I	7	187975	0.8741	N/A	0.5792	-	scaffold_10:1106951-1108537		
I	7	187227	0.4368	N/A	0.6134	(galA) β-1,4-endogalactanase A	scaffold_10:1790462-1791585		
I	7	42683	0.459	N/A	0.3721	-	scaffold_10:357875-358303		
I	7	211963	0.9445	N/A	1.3537	-	scaffold_10:790926-792965		
I	7	212676	1.0068	N/A	1.2515	Flavonol reductase/cinnamoyl-CoA reductase	scaffold_11:1308168-1309423		
I	7	50103	0.7222	N/A	0.8933	Hypothetical, Nucleolar GTPase/ATPase	scaffold_11:635018-637627		
I	7	189925	0.8997	N/A	1.0936	Monocarboxylate transporter	scaffold_12:1204698-1206152		
I	7	203341	2.2761	N/A	2.4079	Fungal specific transcription factor domain	scaffold_12:496315-498768		
I	7	44100	0.3986	N/A	0.3991	unknown. SignalP suggest secreted	scaffold_13:405006-405440		
I	7	213485	0.3697	N/A	0.4293	Cytochrome c heme-binding site	scaffold_14:299354-300904		
I	7	213488	0.8684	N/A	1.1758	-	scaffold_14:308325-309611		
I	7	44563	0.7553	N/A	1.0208	Candidate Phytase gene	scaffold_14:682412-683794		
I	7	44770	0.8484	N/A	1.5052	-	scaffold_15:385693-386159		
I	7	50877	0.4887	N/A	0.6461	Cytochrome b/b6, C-terminal	scaffold_15:478576-480299		
I	7	193892	0.9964	N/A	1.378	-	scaffold_18:349665-350232		
I	7	144265	0.5314	N/A	0.6257	-	scaffold_18:428670-428882		
I	7	45717	1.8277	N/A	2.1337	Isochorismatase hydrolase	scaffold_19:245705-246316		
I	7	137513	0.9374	N/A	1.0697	-	scaffold_19:297524-298076		
I	7	194447	1.6263	N/A	1.6974	putative extracellular GH family 5 cellulase	scaffold_19:399383-400833		
I	7	197387	0.5336	N/A	0.6282	PHK	scaffold_2:1604196-1606989		
I	7	52301	0.486	N/A	0.5418	-	scaffold_2:1842093-1842569		
I	7	173308	0.5553	N/A	0.5122	-	scaffold_2:2940560-2940894		
I	7	52389	1.8695	N/A	2.2287	Chloroperoxidase	scaffold_2:2986700-2987434		
I	7	46081	1.2235	N/A	1.3576	-	scaffold_22:104498-106084		
I	7	46117	1.2972	N/A	1.2104	-	scaffold_24:62939-64723		
I	7	176483	1.4866	N/A	1.7971	12 kDa heat shock protein	scaffold_3:652346-652735		
I	7	135750	0.9858	N/A	0.7971	-	scaffold_3:953551-954314		
I	7	208909	0.6056	N/A	0.7035	-	scaffold_4:1742563-1742997		
I	7	137159	0.9023	N/A	0.9613	-	scaffold_4:2862468-2863401		
I	7	38891	0.5505	N/A	0.5941	hypothetical protein containing fungal specific transcription factor and fungal transcriptional regulatory protein domains.	scaffold_4:744725-747061		
I	7	178492	1.4172	N/A	1.3607	-	scaffold_4:80282-81759	33	
I	7	179912	0.6142	N/A	0.7161	putative extracellular carboxylesterase, type B	scaffold_4:82677-84328	33	
I	7	124156	0.9259	N/A	1.0948	candidate NAD dependent formate dehydrogenase	scaffold_6:131825-133120		
I	7	40747	0.7686	N/A	1.0411	-	scaffold_6:1532032-1532545		
I	7	48710	1.7265	N/A	1.9563	Glutathione-dependent formaldehyde-activating, GFA	scaffold_6:773661-774175		
I	7	127191	0.4243	N/A	0.4741	-	scaffold_7:120748-121779		
I	7	40901	0.6111	N/A	0.8255	Zinc finger protein	scaffold_7:15491-18286		
I	7	53697	0.4438	N/A	0.564	hypothetical protein containing Zn-finger protein, C2H2 type domain	scaffold_7:1555401-1557581		
I	7	128502	0.9826	N/A	0.8984	-	scaffold_7:349396-349722		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
I	7	195355	0.8786	N/A	0.7277	-	scaffold_76:400-1152		
I	7	184942	0.7702	N/A	0.8961	hypothetical AMP-binding enzyme with predicted N-6 Adenine-specific DNA methylase and AMP-dependent synthetase and ligase	scaffold_8:1341042-1342959		
I	7	211004	0.9575	N/A	1.0482	Glycosyl transferase, family 20	scaffold_8:566883-568526		
I	7	42164	0.4026	N/A	0.4372	Oxidoreductase, N-terminal	scaffold_9:433586-435005		
I	8	172298	0.8497	N/A	1.0543	Aromatic-ring hydroxylase	scaffold_1:1931880-1933204		
I	8	35567	0.8291	N/A	1.1657	Ferric reductase-like transmembrane component	scaffold_1:697749-699608		
I	8	35589	0.5089	N/A	0.7058	Flavonol reductase/cinnamoyl-CoA reductase	scaffold_1:770558-771675		
I	8	136869	0.8184	N/A	1.1738	hypothetical lysin. Extracellular. Peptidoglycan-binding domain and peptidase-like domain	scaffold_11:1031253-1031696		
I	8	43846	0.482	N/A	0.6968	Fungal specific transcription factor	scaffold_12:842193-845072		
I	8	190247	0.6926	N/A	1.0321	SWAP mRNA splicing regulator	scaffold_13:796571-797899		
I	8	191368	0.6694	N/A	0.8271	-	scaffold_14:292003-292613		
I	8	50979	0.6193	N/A	0.7836	related to α-L-arabinofuranosidase	scaffold_16:292799-295117		
I	8	204445	0.7896	N/A	1.102	Protein kinase	scaffold_16:597610-599544		
I	8	37273	0.7982	N/A	0.9284	Fungal transcriptional regulatory protein	scaffold_2:2787399-2789221		
I	8	175113	0.7425	N/A	1.0218	Predicted Yippee-type zinc-binding protein	scaffold_2:3989400-3990098		
I	8	46115	0.7586	N/A	0.9481	putative extracellular exo-1,3-beta-D-glucanase with peptidoglycan-binding LysM domain	scaffold_24:51035-55578		
I	8	176378	0.5578	N/A	0.8013	Short-chain dehydrogenase/reductase	scaffold_3:1077907-1078854		
I	8	208129	0.3295	N/A	0.5302	Glycine cleavage H-protein	scaffold_3:2384038-2384713		
I	8	52783	0.7246	N/A	1.0187	Alternative splicing factor SRp55/B52/SRp75 (RRM superfamily)	scaffold_3:3134553-3136488		
I	8	208344	1.2066	N/A	1.7424	Glycoside hydrolase, family 5	scaffold_3:3165320-3166318		
I	8	199253	0.4578	N/A	0.6397	-	scaffold_4:1136529-1137230		
I	8	209060	0.4369	N/A	0.7252	-	scaffold_4:2520615-2522378		
I	8	130770	0.5673	N/A	0.918	-	scaffold_4:571449-573582		
I	8	38924	0.7277	N/A	0.8436	Glycoside hydrolase, family 43	scaffold_4:863806-864848		
I	8	125764	0.7556	N/A	0.9965	-	scaffold_5:1874264-1875004		
I	8	209872	0.3636	N/A	0.5123	Peptidase M3A and M3B	scaffold_5:2027994-2030245		
I	8	41387	0.8391	N/A	1.1847	-	scaffold_7:1607689-1609374		
I	8	56395	1.2112	N/A	1.6653	2-nitropropane dioxygenase	scaffold_7:260908-262184		
I	8	49258	0.603	N/A	0.6292	Hypothetical aldehyde dehydrogenase. May be a succinate-semialdehyde dehydrogenase	scaffold_8:392046-393621		
I	9	54250	0.9066	N/A	1.2936	Dystonin, GAS (Growth-arrest-specific protein), and related proteins	scaffold_10:1908627-1911542		
I	9	51046	0.8206	N/A	1.0172	-	scaffold_16:657687-658458		
I	9	45408	0.6902	N/A	0.7877	-	scaffold_17:551718-552941		
I	9	45265	0.5369	N/A	0.7041	-	scaffold_17:64665-66029		
I	9	214644	0.4537	N/A	0.7462	Putative phosphoinositide phosphatase	scaffold_19:93362-96445		
I	9	206738	0.4845	N/A	0.7837	Esterase/lipase/thioesterase	scaffold_2:1191762-1201345		
I	9	174831	0.5382	N/A	0.8597	Ribonuclease T2	scaffold_2:1760073-1761670		
I	9	55591	0.5434	N/A	0.604	Major facilitator superfamily	scaffold_2:1990464-1992245		
I	9	207209	1.0599	N/A	1.0824	Cytochrome P450	scaffold_2:2863420-2864887		
I	9	52415	1.2187	N/A	1.5291	Glycoside hydrolase, family 38	scaffold_2:3260374-3263874		
I	9	127561	1.2437	N/A	1.4066	-	scaffold_2:3907026-3907502		
I	9	206524	0.6391	N/A	0.7384	-	scaffold_2:523394-525712		
I	9	45928	0.7315	N/A	0.9707	-	scaffold_20:292247-293401		
I	9	57441	1.5438	N/A	2.0224	Hypothetical Sodium/hydrogen exchanger	scaffold_20:62194-65388		
I	9	207626	0.626	N/A	1	-	scaffold_3:521536-522556		
I	9	37926	0.3111	N/A	0.4414	-	scaffold_3:881054-882505		
I	9	53078	0.5194	N/A	0.8342	-	scaffold_4:2646706-2649603		
I	9	199607	0.4738	N/A	0.5467	Phosphatidylinositol-4-phosphate 5-kinase	scaffold_4:2666668-2669402		
I	9	209889	0.8117	N/A	0.9406	-	scaffold_5:2115853-2116700		
I	9	182426	0.9295	N/A	1.1682	hypothetical, ABC transporter	scaffold_6:1936712-1937158		
I	9	53547	1.0766	N/A	1.4797	-	scaffold_6:1965086-1965903		
I	9	40300	1.0581	N/A	1.4455	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_6:45908-47479		
I	9	41345	1.1541	N/A	1.4837	Peptidase C19, ubiquitin carboxyl-terminal hydrolase 2	scaffold_7:1483384-1487376		
I	9	130681	0.5676	N/A	0.914	Fungal specific transcription factor domain	scaffold_7:1520108-1522142		
I	9	201762	0.5778	N/A	0.9027	Predicted ubiquitin-protein ligase/hyperplastic discs protein, HECT superfamily	scaffold_8:1517560-1518774		
I	9	201398	1.0738	N/A	1.2565	-	scaffold_8:278960-282012		
I	9	185354	0.8326	N/A	0.976	Zinc-containing alcohol dehydrogenase	scaffold_8:562931-564490		
I	9	49303	3.3069	N/A	3.7326	Methionine synthase	scaffold_8:671000-672199		
I	10	119858	1.2665	N/A	1.7533	related to α-glucosidase; glycoside hydrolase, family 31	scaffold_1:1038557-1041202		
I	10	35797	0.8555	N/A	1.0203	Gamma-glutamyltranspeptidase	scaffold_1:1380462-1382452		
I	10	46582	0.7349	N/A	1.0984	D-isomer specific 2-hydroxyacid dehydrogenase, NAD-binding	scaffold_1:1951526-1952871		
I	10	196420	0.4747	N/A	0.6113	Hypothetical. Beta-ketoacyl synthase, Zinc-containing alcohol dehydrogenase superfamily	scaffold_1:1985685-1993563		
I	10	52023	0.6539	N/A	0.9911	Adenylosuccinate lyase	scaffold_1:3129762-3131195		
I	10	52038	0.7705	N/A	1.2234	related to D-amino acid oxidase of Fusarium solani	scaffold_1:3247374-3248717		
I	10	212265	1.0847	N/A	1.4161	Hypothetical WW domain protein. Probable involved in signalling cascade	scaffold_10:1943199-1946989		
I	10	43055	0.6354	N/A	1.0605	-	scaffold_10:1984522-1985331		
I	10	120926	1.226	N/A	1.5571	Acyltransferase ChoActase/COT/CPT	scaffold_10:311597-313381		
I	10	203184	1.7245	N/A	1.8229	O-methyltransferase, family 2	scaffold_11:1645152-1646777		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
I	10	188553	0.4096	N/A	0.5412	Acyl-CoA dehydrogenase	scaffold_11:855009-856850		
I	10	212928	1.0472	N/A	1.448	Multidrug/pheromone exporter,	scaffold_12:810285-814322		
I	10	189770	0.673	N/A	0.8599	Short-chain dehydrogenase	scaffold_12:981969-982778		
I	10	192237	0.3979	N/A	0.4827	-	scaffold_15:110057-111261		
I	10	213815	0.8036	N/A	0.967	Cytoskeletal protein A	scaffold_15:669795-670793		
I	10	50981	0.8351	N/A	1.0319	putative AMP-dependent synthetase and ligase, Acyl-CoA synthetase	scaffold_16:313059-315106		
I	10	54874	0.7323	N/A	1.0222	Predicted oxidoreductase	scaffold_16:356267-357604		
I	10	125779	1.2327	N/A	1.3167	-	scaffold_16:542355-543382		
I	10	45131	0.5228	N/A	0.5695	Hypothetical aldehyde dehydrogenase (EC 1.2.1.3).	scaffold_16:549461-551119		
I	10	119078	0.9615	N/A	1.0445	Hypothetical. KOG suggests involvement in RNA processing	scaffold_17:578986-582785		
I	10	214531	0.7211	N/A	1.0567	Major facilitator superfamily	scaffold_18:407944-409447		
I	10	120777	0.6236	N/A	0.8747	-	scaffold_2:1135040-1137018		
I	10	55582	0.8153	N/A	0.9602	Arginase family	scaffold_2:1817410-1818554		
I	10	207027	1.0965	N/A	1.3283	Oxidoreductase, N-terminal	scaffold_2:1944241-1945716		
I	10	52111	3.6217	N/A	3.7908	hypothetical β-galactosidase. extracellular GH family 2	scaffold_2:200167-202439		
I	10	52322	1.9289	N/A	2.6676	-	scaffold_2:2015429-2017439		
I	10	47116	1.9232	N/A	2.0673	Peptidase M14	scaffold_2:3106130-3106978		
I	10	174541	1.3709	N/A	1.7876	Major facilitator superfamily	scaffold_2:394627-396249		
I	10	46947	0.7571	N/A	1.086	Hypothetical acetyl-CoA acetyltransferase	scaffold_2:871918-873471		
I	10	174413	1.1121	N/A	1.5277	Candidate galactose-1-phosphate uridyl transferase	scaffold_2:928571-929921	34	
I	10	136140	0.8166	N/A	1.3793	-	scaffold_2:930673-931707	34	
I	10	55161	0.547	N/A	0.8547	Hypothetical Alpha/beta hydrolase. Involded in aromatic compound metabolism	scaffold_20:130487-131602		
I	10	177616	2.3474	N/A	3.0802	Sugar transporter superfamily	scaffold_3:115239-116759		
I	10	52684	0.5586	N/A	0.8578	Predicted carbohydrate kinase	scaffold_3:2122838-2124319		
I	10	208214	0.8526	N/A	1.0735	related to 1,3-beta-glucanosyltransferase	scaffold_3:2755219-2756323		
I	10	129458	0.8344	N/A	1.1872	-	scaffold_3:394227-397602		
I	10	47796	0.5093	N/A	0.7061	Haloacid dehalogenase-like hydrolase	scaffold_4:214532-215500		
I	10	179322	0.4756	N/A	0.6047	Hypothetical protein	scaffold_4:2563972-2565542		
I	10	178744	1.1116	N/A	1.5498	Hypothetical Metal-dependent phosphohydrolase, HD region	scaffold_4:2610303-2611352		
I	10	39990	1.338	N/A	1.6642	Carbamoyl-phosphate synthetase large chain	scaffold_5:1475905-1478449		
I	10	181202	0.4763	N/A	0.7853	-	scaffold_5:1525014-1526550		
I	10	209771	0.9628	N/A	1.2286	-	scaffold_5:1732793-1734572		
I	10	180211	0.6204	N/A	0.8511	Alpha/beta hydrolase	scaffold_5:821074-821908		
I	10	56177	0.9276	N/A	1.0753	Hypothetical alcohol dehydrogenase	scaffold_5:850675-852127		
I	10	41258	1.3375	N/A	1.5677	-	scaffold_7:1162534-1163028		
I	10	184312	1.6982	N/A	2.1309	Glutathione S-transferase	scaffold_7:116722-117637		
I	10	40935	0.5349	N/A	0.7	hypothetical prolyl aminopeptidase	scaffold_7:122815-123816		
I	10	41385	0.6461	N/A	0.7491	Major facilitator superfamily	scaffold_7:1603850-1605521		
I	10	210782	0.8291	N/A	0.9457	-	scaffold_7:1615053-1615892		
I	10	210569	0.6268	N/A	1.0324	Uncharacterized conserved protein	scaffold_7:544741-546048		
I	10	183329	1.0879	N/A	1.1836	-	scaffold_7:979958-981169		
I	10	201877	0.6053	N/A	0.7925	(glkA) glucokinase	scaffold_9:257427-258973		
I	11	46405	2.8132	N/A	3.1421	-	scaffold_1:1042507-1043734		
I	11	205517	1.6151	N/A	1.5573	msdS, α-1,2-mannosidase S	scaffold_1:643984-645577		
I	11	50237	2.8043	N/A	2.993	Hypothetical Potassium/sodium efflux P-type ATPase	scaffold_11:1534505-1538847		
I	11	136363	1.038	N/A	1.1865	-	scaffold_11:1642055-1642656		
I	11	122657	0.8722	N/A	0.808	-	scaffold_12:621737-623065		
I	11	132291	1.8646	N/A	2.0972	Sugar (ANd other) transporter	scaffold_12:906166-907847		
I	11	213014	1.812	N/A	2.0009	Flavin-containing monooxygenase	scaffold_13:137479-139378		
I	11	50710	0.6327	N/A	0.6954	-	scaffold_14:420369-421225		
I	11	204047	2.1527	N/A	1.9887	TGF-beta receptor, type I/II extracellular region	scaffold_14:864802-866927		
I	11	191792	0.5485	N/A	0.5624	Mandelate racemase	scaffold_15:227279-228669		
I	11	213766	1.5457	N/A	1.593	-	scaffold_15:366330-368172		
I	11	193806	0.3802	N/A	0.4412	hypothetical carboxylesterase (type B) with signal peptide motif	scaffold_18:312599-314247		
I	11	194014	0.8299	N/A	0.8827	Amino acid/polyamine transporter I	scaffold_18:354031-356372		
I	11	47044	1.5762	N/A	1.7337	Dihydrodipicolinate synthetase family	scaffold_2:1946374-1947381		
I	11	197549	0.9944	N/A	1.0056	Sugar (ANd other) transporter	scaffold_2:2041969-2043781		
I	11	36645	2.3051	N/A	2.4681	NRPS	scaffold_2:245518-248837		
I	11	119946	0.5773	N/A	0.6319	AAA ATPase	scaffold_3:678446-680771		
I	11	209012	1.4142	N/A	1.6	Proteins containing the FAD binding domain	scaffold_4:2426928-2428844		
I	11	55928	0.6833	N/A	0.7089	Aldo/keto reductase family proteins	scaffold_4:329060-330435		
I	11	208583	0.9109	N/A	0.835	-	scaffold_4:344296-345421		
I	11	48541	0.5363	N/A	0.6001	Peptidase S15	scaffold_5:2140556-2142455		
I	11	40596	0.9698	N/A	0.9541	Aldehyde dehydrogenase	scaffold_6:1072547-1074178		
I	11	182312	1.3771	N/A	1.4674	UreD urease accessory protein	scaffold_6:1616393-1617463		
I	11	53523	2.015	N/A	2.0285	Dihydroxy-acid and 6-phosphogluconate dehydratase	scaffold_6:1689681-1691759		
I	11	40429	0.7634	N/A	0.8292	Mpv17 / PMP22 family	scaffold_6:546382-547191		
I	11	183753	1.8672	N/A	2.0335	Related to Hypocrea jecorina D-galacturonic acid reductase	scaffold_7:380770-381898		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
I	11	49422	1.2458	N/A	1.2719	Hypothetical NADH:flavin oxidoreductase/NADH oxidase	scaffold_8:1366571-1367948		
I	11	210842	1.5723	N/A	1.6374	Cytochrome c heme-binding site	scaffold_8:58091-59659		
I	11	211032	2.3927	N/A	2.2373	hypothetical tripeptidyl peptidase	scaffold_8:629512-631485		
I	12	46429	0.6393	N/A	0.8055	Glycosyl hydrolases family 35	scaffold_1:1168270-1171598		
I	12	187366	0.7425	N/A	1.3017	AMP-binding enzyme	scaffold_10:884067-886122		
I	12	202490	0.4703	N/A	0.5442	Cellulase (glycosyl hydrolase family 5)	scaffold_10:970771-972141		
I	12	54380	1.0031	N/A	1.2646	-	scaffold_11:1020871-1022568		
I	12	189170	0.8461	N/A	1.2223	Related to α keto acid dehydrogenase complex of Aspergillus fumigatus; EC 2.3.1.12	scaffold_11:1114386-1116012		
I	12	188806	0.8249	N/A	1.0713	Acyl-CoA synthetase	scaffold_11:1306168-1307932		
I	12	54297	0.7231	N/A	1.2691	Predicted L-carnitine dehydratase/alpha-methylacyl-CoA racemase	scaffold_11:184930-186148		
I	12	43297	1.1448	N/A	1.4609	Glyoxylate/hydroxypyruvate reductase (D-isomer-specific 2-hydroxy acid dehydrogenase superfamily)	scaffold_11:813729-814975		
I	12	189342	0.8048	N/A	0.9951	Sugar transporter	scaffold_12:1093588-1095397		
I	12	189463	0.6981	N/A	0.8766	-	scaffold_12:54028-55185		
I	12	43857	1.0886	N/A	1.4623	Amino acid permease	scaffold_12:892056-893696		
I	12	54651	0.7135	N/A	1.0719	hypothetical 3-ketoacyl-CoA-thiolase	scaffold_13:1053628-1055053		
I	12	213369	0.6813	N/A	0.9903	-	scaffold_13:1146976-1148211		
I	12	54693	1.0991	N/A	1.2945	-	scaffold_14:202423-203986		
I	12	44729	0.7118	N/A	1.1188	Zinc-containing alcohol dehydrogenase superfamily	scaffold_15:232440-233775		
I	12	44808	0.6994	N/A	1.0877	Acetyl-CoA acetyltransferase	scaffold_15:488847-490223		
I	12	192093	0.7702	N/A	0.8649	Major facilitator superfamily	scaffold_15:675841-677552		
I	12	120468	0.4078	N/A	0.6795	Fungal specific transcription factor	scaffold_15:878961-881192		
I	12	139793	1.1322	N/A	1.3038	Fungal specific transcription factor	scaffold_17:190366-192210		
I	12	55019	1.0369	N/A	1.2126	-	scaffold_17:548417-549115		
I	12	45504	0.8781	N/A	1.3405	-	scaffold_18:212650-213765		
I	12	121007	0.5111	N/A	0.7222	-	scaffold_19:357653-359649		
I	12	174315	0.921	N/A	1.5272	-	scaffold_2:1172316-1175896		
I	12	175036	0.6883	N/A	0.9064	-	scaffold_2:1235088-1236189		
I	12	36613	0.8344	N/A	1.0779	-	scaffold_2:138188-138709		
I	12	174330	1.2747	N/A	1.8037	Major facilitator superfamily	scaffold_2:1915524-1917758		
I	12	55604	0.7975	N/A	1.0747	-	scaffold_2:2644899-2646257		
I	12	174633	0.4607	N/A	0.6242	Fungal transcriptional regulatory protein, N-terminal	scaffold_2:697979-700258		
I	12	36816	0.9124	N/A	1.0785	AMP-dependent synthetase and ligase	scaffold_2:874739-876892		
I	12	51404	0.344	N/A	0.5562	protein with RA domain	scaffold_20:67362-68976		
I	12	47390	0.4845	N/A	0.8326	-	scaffold_3:1352791-1354209		
I	12	55668	0.7603	N/A	1.0761	Sugar transporter	scaffold_3:366663-371900		
I	12	55671	0.4741	N/A	0.5467	Oxoprolinase	scaffold_3:390001-393891		
I	12	176553	0.5915	N/A	0.7771	-	scaffold_3:517527-519436		
I	12	55680	1.2498	N/A	1.7552	Coenzyme A transferase	scaffold_3:571644-573322		
I	12	38750	0.4752	N/A	0.6566	-	scaffold_4:238480-239802		
I	12	209032	1.6526	N/A	2.0714	-	scaffold_4:2475468-2476710		
I	12	52848	0.8336	N/A	1.1205	-	scaffold_4:35438-36198		
I	12	180608	0.8904	N/A	1.1996	-	scaffold_5:1465619-1466701		
I	12	181451	0.9232	N/A	1.137	Hypothetical 3-methylcrotonyl-CoA carboxylase, subunit β	scaffold_5:1482203-1483993		
I	12	56260	0.4905	N/A	0.6519	Fungal specific transcription factor	scaffold_5:2300403-2304019		
I	12	39667	0.8492	N/A	1.2204	-	scaffold_5:334506-335735		
I	12	180923	1.4503	N/A	1.8185	Major facilitator superfamily	scaffold_5:907159-909074		
I	12	200686	0.908	N/A	1.4125	Predicted transporter (major facilitator superfamily)	scaffold_6:1038217-1039971		
I	12	210238	1.1039	N/A	1.4009	-	scaffold_6:1183869-1184234		
I	12	53660	0.8583	N/A	1.0378	-	scaffold_7:1059596-1061058		
I	12	53563	1.2394	N/A	1.5681	Mandelate racemase/muconate lactonizing enzyme	scaffold_7:251219-252764		
I	12	49321	0.7501	N/A	1.0393	-	scaffold_8:747044-749231		
I	12	42079	0.8345	N/A	1.05	-	scaffold_9:168222-169710		
J	1	55296	N/A	-0.728	0.524	Hypothetical threonyl-tRNA synthetase kinase. HMMPfam indicates Threonyl-tRNA synthetase kinase activity	scaffold_1:1025077-1026657		
J	1	46431	N/A	-0.6354	0.4153	Predicted translation product shares amino acid sequence similarity to the Saccharomyces cerevisiae PUS7 gene product; pseudouridine synthase, catalyzes pseudouridylation at position 35 in U2 snRNA, position 13 in cytoplasmic tRNAs, and position 35 in pre-tRNA(Tyr).	scaffold_1:1187016-1189287		
J	1	172862	N/A	-1.6319	0.8708	Hypothetical formamidopyrimidine-DNA glycolase	scaffold_1:1910410-1911593		
J	1	205975	N/A	-0.4789	0.3532	GTPase Rab11/YPT3, small G protein superfamily	scaffold_1:2186803-2187743		
J	1	196499	N/A	-1.0664	0.8249	Major facilitator superfamily	scaffold_1:2233327-2235188		
J	1	143893	N/A	-1.0321	0.8028	-	scaffold_1:2304516-2304704		
J	1	206025	N/A	-0.6653	0.5277	Actin-related protein	scaffold_1:2315308-2316503		
J	1	36121	N/A	-1.0594	0.627	-	scaffold_1:2364923-2365480		
J	1	172313	N/A	-0.9294	0.7371	dUTPase	scaffold_1:2424429-2425171		
J	1	35463	N/A	-0.8998	0.6485	-	scaffold_1:312669-314372		
J	1	36288	N/A	-0.7099	0.4311	-	scaffold_1:3151987-3152791		
J	1	46776	N/A	-0.7755	0.5245	TatD-related DNase	scaffold_1:3201614-3202795		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	1	55495	N/A	-1.1234	0.9187	Zn-finger, C2H2 type	scaffold_1:3674444-3677114		
J	1	171303	N/A	-0.8635	0.6242	-	scaffold_1:3965181-3968583		
J	1	46331	N/A	-0.6465	0.5699	Hypothetical dihydrouridine synthase	scaffold_1:580308-582653		
J	1	35583	N/A	-0.5276	0.439	Deduced amino acid sequence shares identity with the Saccharomyces cerevisiae NCL1 gene product; an S-adenosyl-L-methionine-dependent tRNA: m5C-methyltransferase; methylates cytosine to m5C at several positions in tRNAs and intron-containing pre-tRNAs.	scaffold_1:753837-756709		
J	1	187914	N/A	-1.0837	0.8355	-	scaffold_10:1157702-1158739		
J	1	56817	N/A	-0.4961	0.3248	Candidate RmtA	scaffold_10:1210100-1211443		
J	1	56837	N/A	-0.8043	0.4334	Ribosomal protein L24	scaffold_10:1831947-1833063		
J	1	187681	N/A	-0.5403	0.414	-	scaffold_10:1961922-1962354	35	
J	1	143164	N/A	-0.7	0.4768	Transcriptional regulator	scaffold_10:1965699-1966166	35	
J	1	56855	N/A	-0.7404	0.5091	Hypothetical protein with SAM (and some other nucleotide) binding motif	scaffold_10:1978886-1979797		
J	1	126891	N/A	-0.6695	0.571	Molybdopterin cofactor biosynthesis protein	scaffold_11:1028413-1028925		
J	1	189264	N/A	-0.5148	0.3218	-	scaffold_11:1445270-1446494		
J	1	130008	N/A	-0.9483	0.5911	(apsB) aminopeptidase B	scaffold_11:36071-39418		
J	1	54436	N/A	-0.7015	0.5099	Splicing coactivator SRm160	scaffold_12:19195-21140		
J	1	54483	N/A	-0.5235	0.3469	Related to squalene synthetase (EC 2.5.1.21). Involved in lipid biosynthesis.	scaffold_12:501468-503073		
J	1	56974	N/A	-0.8149	0.5964	Hypothetical G-protein with WD-40 repeats	scaffold_12:95355-96682		
J	1	203834	N/A	-0.9717	0.5615	Alkyl hydroperoxide reductase, thiol specific antioxidant and related enzymes	scaffold_13:1196963-1197775		
J	1	50449	N/A	-0.4191	0.3418	hypothetical RNA procesing protein	scaffold_13:221279-223698		
J	1	122186	N/A	-0.7225	0.6533	G-patch nucleic acid binding protein	scaffold_13:697881-699507		
J	1	50555	N/A	-0.8774	0.6058	Hypothetical Polyadenylate-binding protein (RRM superfamily	scaffold_13:713576-714673		
J	1	44238	N/A	-0.721	0.4086	DEAD/DEAH box helicase	scaffold_13:785519-787324		
J	1	213243	N/A	-0.768	0.5898	Related to MTR4 DEAD-box family ATP-dependent helicase.	scaffold_13:802759-806271	36	
J	1	213247	N/A	-0.5878	0.3676	-	scaffold_13:806648-811946	36	
J	1	44253	N/A	-0.6502	0.3239	-	scaffold_13:834287-835135		
J	1	57102	N/A	-0.8949	0.4801	Ribonucleotide reductase large subunit	scaffold_13:941867-944676		
J	1	213313	N/A	-0.8115	0.5207	-	scaffold_13:956727-957425		
J	1	213466	N/A	-0.6854	0.4894	Peptidase	scaffold_14:273454-281114		
J	1	191097	N/A	-0.6816	0.5011	Ribosomal protein S16	scaffold_14:354940-355328		
J	1	44607	N/A	-0.749	0.4678	Hypothetical sulfatase	scaffold_14:837876-839840		
J	1	213417	N/A	-0.5402	0.3446	-	scaffold_14:85988-87091		
J	1	54784	N/A	-0.6126	0.3384	-	scaffold_15:153624-154946		
J	1	51140	N/A	-0.5386	0.3731	Hypothetical Signal recognition particle, subunit Srp72	scaffold_17:196692-198853		
J	1	204746	N/A	-0.6316	0.4092	Phosphoribosyl pyrophosphate synthetase	scaffold_17:415702-416878		
J	1	45634	N/A	-1.1467	0.684	Hypothetical. Ankyrin repeat	scaffold_19:13477-16140		
J	1	194526	N/A	-1.0897	0.6396	putative extracellular HpcH/HpaI aldolase	scaffold_19:140164-141142		
J	1	45645	N/A	-0.8451	0.6954	-	scaffold_19:43783-45437		
J	1	121703	N/A	-1.0952	0.8822	hypothetical histone acetyltransferase type b catalytic subunit	scaffold_2:1063334-1064950		
J	1	46970	N/A	-1.2735	0.9554	AAA ATPase	scaffold_2:1123355-1124707		
J	1	173325	N/A	-0.6154	0.4269	-	scaffold_2:1270082-1270634		
J	1	173056	N/A	-0.7358	0.5029	Ribosomal protein L13	scaffold_2:1506342-1507098		
J	1	174983	N/A	-0.744	0.4732	Predicted methyltransferase	scaffold_2:1581797-1582961		
J	1	37044	N/A	-0.6265	0.5431	Related to anti-silencing protein ASF1	scaffold_2:1695213-1696243		
J	1	52321	N/A	-1.6202	1.1813	-	scaffold_2:2005692-2006180		
J	1	37140	N/A	-1.0587	0.7599	-	scaffold_2:2018065-2019117		
J	1	175143	N/A	-0.8425	0.7119	Transcription factor with Homeobox domains	scaffold_2:2034791-2036677		
J	1	130199	N/A	-0.5015	0.3805	Hypothetical 5′-3′ exonuclease	scaffold_2:2648953-2650581		
J	1	52363	N/A	-0.6242	0.4135	Hypothetical ribose-phosphate pyrophosphokinase	scaffold_2:2670131-2671532		
J	1	55611	N/A	-0.5148	0.3807	putative eIF2 α subunit, similar to Gcn3p of S. cerevisiae. possibly involved in translation initiation and protein biosynthesis.	scaffold_2:2701874-2703003		
J	1	143657	N/A	-0.9306	0.6207	Hypothetical Zn-finger protein	scaffold_2:3049802-3050505		
J	1	207297	N/A	-0.5542	0.4366	Tyrosine protein kinase	scaffold_2:3231169-3233559		
J	1	47138	N/A	-1.1229	0.9981	AAA ATPase	scaffold_2:3318290-3321187		
J	1	37431	N/A	-0.8003	0.5294	hypothetical protein with predicted helicase, DEAD/DEAH-box and SNF-2 related domain; KOG Class: Chromatin structure and dynamics; KOG Id: 0389; KOG description: hypothetical protein predicted to have Cyclin-like F-box and transcription factor jumonji, jmjC; domains; KOG Class: Chromatin structure and dynamics; KOG Id: 2130; KOG description: SNF2 family DNA-dependent ATPase	scaffold_2:3327748-3331119		
J	1	37485	N/A	-1.109	0.7287	-	scaffold_2:3498562-3499036		
J	1	134398	N/A	-0.6291	0.3874	putative GH family 43 protein with 47% sequence identity to an Aspergillus nidulans endo-arabinanase (PMID: 16844780)	scaffold_2:370064-371373		
J	1	124776	N/A	-0.8252	0.7446	Cytidine/deoxycytidylate deaminase	scaffold_2:3996432-3997811		
J	1	175045	N/A	-0.7407	0.5907	Deduced amino acid sequence shares identity with mitochondrial 21S rRNA methyltransferase, required for methylation of U(2791) in 21S rRNA; has similarity to Spb1p and Trm7p, and to E. coli FtsJ/RrmJ.	scaffold_2:4004506-4005670		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	1	36725	N/A	-0.5356	0.4191	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae RRP42 gene product; a protein involved in rRNA processing; component of the exosome 3->5 exonuclease complex with Rrp4p, Rrp41p, Rrp43p and Dis3p.	scaffold_2:518188-519410		
J	1	197120	N/A	-0.7751	0.4458	Ribosomal protein L29	scaffold_2:794307-795153		
J	1	38117	N/A	-1.0433	0.7926	Single-stranded DNA-binding replication protein A (RPA), medium (30 kD) subunit	scaffold_3:1618882-1619956		
J	1	38157	N/A	-0.5589	0.4824	-	scaffold_3:1762637-1765219		
J	1	175900	N/A	-0.6423	0.4638	GCN5-related N-acetyltransferase	scaffold_3:2410029-2410941		
J	1	38426	N/A	-0.6407	0.4495	Short-chain dehydrogenase/reductase	scaffold_3:2800319-2801444		
J	1	176593	N/A	-1.1926	0.8738	Transmembrane amino acid transporter protein	scaffold_3:2923789-2925440		
J	1	175742	N/A	-0.8034	0.6379	hypothetical WD-40 repeat and TUP1 like protein; KOG Class: Cell cycle control, cell division, chromosome partitioning; KOG Id: 0973; KOG description: Histone transcription regulator HIRA, WD repeat superfamily	scaffold_3:3240448-3243651		
J	1	38566	N/A	-0.5491	0.3886	Hypothetical. RNA splicing. Related to S. cerev.TRL, tRNA ligase, required for tRNA splicing	scaffold_3:3269476-3271941		
J	1	128714	N/A	-0.905	0.6311	Candidate Rad54 homolog (first part); Related to Vac14 homolog (second part)	scaffold_3:767719-774314		
J	1	47328	N/A	-0.5765	0.4368	Magnesium-dependent phosphatase	scaffold_3:828757-829476		
J	1	141499	N/A	-0.9002	0.6734	Protein kinase	scaffold_4:1360010-1360995		
J	1	53035	N/A	-0.6747	0.4398	Phosphoribulokinase/uridine kinase	scaffold_4:2371423-2373230		
J	1	178578	N/A	-0.8087	0.4036	Phospholipase/carboxyhydrolase	scaffold_4:2482040-2482825		
J	1	48158	N/A	-0.9381	0.762	Related to DNA-repair protein rad2 from S. pombe	scaffold_4:2677459-2678939		
J	1	199092	N/A	-0.9766	0.8238	-	scaffold_4:423410-424072		
J	1	135359	N/A	-1.1183	0.8687	-	scaffold_5:1530049-1531080		
J	1	180383	N/A	-0.3675	0.2913	Thiamine pyrophosphokinase	scaffold_5:1827592-1828798		
J	1	209842	N/A	-0.754	0.5043	Phosphoribosyl pyrophosphate synthetase	scaffold_5:1964240-1965992		
J	1	181254	N/A	-0.5723	0.4405	Hypothetical phosphatidate cytidylyltransferase	scaffold_5:206868-208387		
J	1	200368	N/A	-0.562	0.4282	-	scaffold_5:2130904-2131686		
J	1	180652	N/A	-1.8226	0.9273	-	scaffold_5:2157900-2158940		
J	1	180548	N/A	-1.1221	0.6784	-	scaffold_5:2332493-2333314		
J	1	48261	N/A	-0.8447	0.6621	Predicted hydrolase	scaffold_5:277132-278410		
J	1	56136	N/A	-0.7167	0.4256	Peptidase	scaffold_5:328035-329363	37	
J	1	199843	N/A	-0.8615	0.5392	Aromatic-ring hydroxylase	scaffold_5:329940-331578	37	
J	1	180664	N/A	-0.6738	0.4462	Ribosomal protein S8	scaffold_5:339002-339514		
J	1	39731	N/A	-0.6803	0.5358	-	scaffold_5:599723-600200		
J	1	48367	N/A	-0.8393	0.6171	DNA topoisomerase	scaffold_5:891206-893426		
J	1	182791	N/A	-0.8289	0.5658	Predicted telomere binding protein	scaffold_6:1626642-1628679		
J	1	127270	N/A	-1.3591	0.9166	-	scaffold_6:168323-169003		
J	1	128031	N/A	-0.7141	0.4597	-	scaffold_6:1720095-1720619		
J	1	48618	N/A	-0.9979	0.7983	Esterase/lipase/thioesterase	scaffold_6:212961-214609		
J	1	48584	N/A	-0.5707	0.3658	ABC transporter	scaffold_6:86866-87774	38	
J	1	48585	N/A	-0.6877	0.5231	Shares amino acid sequence identity to the yeast delta 2-isopentenyl pyrophosphate:tRNA isopentenyl transferase, required for biosynthesis of the modified base isopentenyladenosine in mitochondrial and cytoplasmic tRNAs.	scaffold_6:88190-89758	38	
J	1	49138	N/A	-1.0255	0.6697	AAA ATPase	scaffold_7:1456089-1457398		
J	1	125999	N/A	-0.5629	0.4036	Cytosine deaminase FCY1 and related enzymes	scaffold_7:301695-302937		
J	1	41074	N/A	-1.1927	0.9283	-	scaffold_7:574679-575491		
J	1	53636	N/A	-0.9867	0.811	DNA-directed DNA polymerase B	scaffold_7:792593-799401		
J	1	49072	N/A	-1.367	1.0375	Eukaryotic-type DNA primase, catalytic (small) subunit	scaffold_7:900478-902138		
J	1	184431	N/A	-0.4499	0.3675	DEAD box containing helicases	scaffold_8:131309-135750		
J	1	56635	N/A	-1.0645	0.7213	Ribonucleotide reductase	scaffold_8:1644605-1646032		
J	1	49219	N/A	-1.1615	0.8175	Hypothetical thymidylate synthase or queunine-tRNA ribosyl transferase	scaffold_8:165034-167936		
J	1	41458	N/A	-1.4582	1.1029	-	scaffold_8:25224-26154		
J	1	49331	N/A	-0.6533	0.3994	Predicted methyltransferase	scaffold_8:837226-838359		
J	1	211116	N/A	-1.2749	0.8689	Possible DNA replication licensing factor	scaffold_8:945344-948407		
J	1	53826	N/A	-0.9552	0.5002	Glycosyl transferase, family 15	scaffold_8:992553-993885		
J	1	42394	N/A	-0.8255	0.4457	MCM protein 4	scaffold_9:1100102-1103401		
J	1	186220	N/A	-1.5116	1.055	ATP-dependent DNA ligase	scaffold_9:1112805-1115652		
J	1	133913	N/A	-0.5462	0.3928	-	scaffold_9:1254306-1255628		
J	1	186837	N/A	-0.5501	0.3644	-	scaffold_9:1292938-1293459		
J	1	201939	N/A	-1.0872	0.8561	Phospholipase/carboxyhydrolase	scaffold_9:428085-428931		
J	2	51820	N/A	-0.8059	0.6013	Related to S. cerevisiae phosphatidyl serine synthase	scaffold_1:1353223-1355698		
J	2	170122	N/A	-0.9844	0.7616	Predicted BRCT domain protein	scaffold_1:1832481-1835250		
J	2	205376	N/A	-1.1091	0.6573	-	scaffold_1:205208-206870		
J	2	205573	N/A	-1.2924	0.9614	unknown, has cyclin-like F box	scaffold_1:825823-826444		
J	2	35620	N/A	-1.0603	0.735	Peptidase M19	scaffold_1:865812-867266		
J	2	212062	N/A	-0.5499	0.3839	Deduced amino acid sequence shares identity with the Saccharomyces cerevisiae RBG1 gene product; a member of the DRG family of GTP-binding proteins; interacts with translating ribosomes.	scaffold_10:1054903-1056371		
J	2	212155	N/A	-0.643	0.4068	Ribosomal protein S2	scaffold_10:1705803-1707058		
J	2	187304	N/A	-0.8136	0.508	Ergosterol biosynthesis ERG4/ERG24 family	scaffold_10:795630-797224		
J	2	211974	N/A	-0.8107	0.4631	-	scaffold_10:816365-817361		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	2	127767	N/A	-0.8489	0.5743	Peroxisomal membrane protein MPV17 and related proteins	scaffold_11:1157074-1157771		
J	2	212314	N/A	-0.8127	0.6024	related to Byr4p (a regulator of septation in S. pombe)	scaffold_11:15108-18121		
J	2	43232	N/A	-0.7125	0.522	-	scaffold_11:560679-562592		
J	2	123683	N/A	-0.701	0.4677	Esterase/lipase/thioesterase	scaffold_12:1079971-1081391		
J	2	134406	N/A	-1.1771	0.795	-	scaffold_12:166846-168165		
J	2	190334	N/A	-0.9982	0.6557	Major facilitator superfamily	scaffold_13:141866-143787		
J	2	190628	N/A	-0.5856	0.4234	hypothetical HSA-Myb protein	scaffold_13:692367-697156		
J	2	213505	N/A	-1.3014	0.9067	Haloacid dehalogenase-like hydrolase	scaffold_14:335849-336649		
J	2	50698	N/A	-1.1121	0.8656	Hypothetical. Calcium/actin binding	scaffold_14:343070-345349		
J	2	204569	N/A	-1.4758	1.1006	-	scaffold_16:888066-889617		
J	2	214261	N/A	-0.8859	0.5264	two-component signal transduction system	scaffold_17:256309-256772		
J	2	51205	N/A	-0.6171	0.4625	-	scaffold_17:540441-542338		
J	2	214410	N/A	-0.7036	0.4318	AAA ATPase	scaffold_17:645389-647553		
J	2	194528	N/A	-0.5114	0.2854	-	scaffold_19:123953-124261		
J	2	120104	N/A	-1.0649	0.7189	candidate β-N-acetylglucosaminidase	scaffold_2:1909574-1912259		
J	2	173099	N/A	-1.0496	0.7005	Esterase/lipase/thioesterase	scaffold_2:2076214-2077662		
J	2	207163	N/A	-0.7974	0.5364	Sulfate/bicarbonate/oxalate exchanger SAT-1 and related transporters	scaffold_2:2695680-2698068		
J	2	52374	N/A	-1.1764	0.8844	hypothetical protein with ankyrin and DNA-binding domains	scaffold_2:2780149-2782401		
J	2	37453	N/A	-0.6371	0.4983	multiprotein-bridging factor 1, MBF1. Combines diff. transcriptional coactivators	scaffold_2:3395259-3395805		
J	2	206486	N/A	-0.5683	0.444	hypothetical protein with predicted peptidase S10 and N-6 Adenine-specific DNA methylase;	scaffold_2:447070-454233		
J	2	36714	N/A	-1.1369	0.7306	hypothetical diadenosine and diphosphoinositol polyphosphate phosphohydrolase	scaffold_2:485913-486536		
J	2	173825	N/A	-0.7624	0.5975	Candidate Alpha-1,2 glucosyltransferase alg10	scaffold_2:772315-774230		
J	2	208023	N/A	-0.682	0.432	-	scaffold_3:2051636-2052838		
J	2	177314	N/A	-0.6877	0.4852	Initiation factor 3	scaffold_3:2371175-2371864		
J	2	198936	N/A	-0.7376	0.3947	Hypothetical protein with PPR repeat	scaffold_3:3418107-3419984		
J	2	52824	N/A	-0.5376	0.3511	-	scaffold_3:3447419-3448759		
J	2	38648	N/A	-0.558	0.4021	G-like protein containing WD-40 repeat. Some similarity to A. nidulans SonA	scaffold_3:3509101-3510248		
J	2	37809	N/A	-0.866	0.5828	-	scaffold_3:486196-487338		
J	2	47987	N/A	-1.217	0.6912	Isoflavone reductase	scaffold_4:1447131-1448371		
J	2	179830	N/A	-0.6232	0.3147	Peptidase M, neutral zinc metallopeptidases, zinc-binding site	scaffold_4:1557450-1561711		
J	2	178971	N/A	-0.6388	0.3809	Actin-binding protein SLA2/Huntingtin-interacting protein Hip1	scaffold_4:2641932-2645682		
J	2	56096	N/A	-0.7452	0.4691	-	scaffold_4:2886237-2890167		
J	2	47812	N/A	-0.4757	0.338	OPT oligopeptide transporter protein	scaffold_4:308469-313567		
J	2	142990	N/A	-0.8657	0.6782	mRNA splicing factor	scaffold_5:1348765-1349517		
J	2	209700	N/A	-0.9428	0.5766	ABC transporter	scaffold_5:1553965-1559033		
J	2	209300	N/A	-0.6219	0.4082	-	scaffold_5:182879-184186		
J	2	53348	N/A	-1.4095	0.9211	-	scaffold_5:2047336-2051208		
J	2	40159	N/A	-1.3901	0.7784	-	scaffold_5:2075292-2076252		
J	2	39630	N/A	-0.5138	0.3592	Ribosomal protein S4	scaffold_5:213715-215271		
J	2	56149	N/A	-0.9246	0.5078	Metallophosphoesterase	scaffold_5:495519-497283		
J	2	209436	N/A	-0.7933	0.5795	putative cell polarity protein	scaffold_5:569867-572722		
J	2	200706	N/A	-0.6653	0.5552	-	scaffold_6:1162300-1163152		
J	2	200760	N/A	-1.0938	0.7115	hypothetical gamma interferon inducible lysosomal thiol reductase	scaffold_6:1501797-1502832		
J	2	53520	N/A	-0.577	0.423	Ras1 guanine nucleotide exchange factor	scaffold_6:1674077-1677954		
J	2	53364	N/A	-1.5934	1.2029	related to aspartic protease	scaffold_6:3030-4629		
J	2	181825	N/A	-0.642	0.4317	Nuclear cap-binding complex, subunit NCBP1/CBP80	scaffold_6:62306-65386		
J	2	200640	N/A	-0.8308	0.5009	-	scaffold_6:826155-827404		
J	2	200652	N/A	-0.7943	0.5507	C-3 sterol dehydrogenase/3-beta-hydroxysteroid dehydrogenase and related dehydrogenases	scaffold_6:871765-873062		
J	2	185280	N/A	-0.7394	0.4109	-	scaffold_8:1028971-1030535		
J	2	184522	N/A	-0.8798	0.6958	Hypothetical DNA polymerase	scaffold_8:1484216-1486315		
J	2	211068	N/A	-0.9184	0.6508	-	scaffold_8:771113-773579		
J	2	136122	N/A	-1.059	0.6598	Hypothetical Ubiquinol cytochrome c reductase assembly protein CBP3	scaffold_9:1633411-1634205		
J	2	49553	N/A	-1.0958	0.7097	Hypothetical acetyltransferase	scaffold_9:412480-413083		
J	2	42312	N/A	-0.8205	0.6287	-	scaffold_9:856947-858988		
J	3	171442	N/A	-0.579	0.3898	-	scaffold_1:2023679-2024973		
J	3	196617	N/A	-0.6732	0.4387	GCN5-related N-acetyltransferase	scaffold_1:2756439-2757222		
J	3	172191	N/A	-1.1805	0.8301	-	scaffold_1:3157388-3158751		
J	3	205431	N/A	-0.9597	0.7099	Molecular chaperones HSP70/HSC70, HSP70 superfamily	scaffold_1:407821-410181		
J	3	205501	N/A	-0.6203	0.3576	Hypothetical cell division cycle protein	scaffold_1:597707-599683		
J	3	125165	N/A	-0.6581	0.3609	Hypothetical protein with GAT domain	scaffold_1:684587-685522		
J	3	205572	N/A	-1.3812	0.993	hypothetical protein containing Zn-finger, C2H2 type and U1-like domains	scaffold_1:824493-825149		
J	3	54192	N/A	-0.6915	0.412	Sterol O-acyltransferase	scaffold_10:1115249-1117155		
J	3	186950	N/A	-0.8712	0.5639	-	scaffold_10:454081-456202		
J	3	42800	N/A	-1.0271	0.6769	-	scaffold_10:751352-751837		
J	3	54419	N/A	-0.8305	0.5506	-	scaffold_11:1527990-1529585		
J	3	212403	N/A	-1.2445	0.7968	Possible combined gene model comprising a homologue of S. cerevisiae SEN2 on the 5′ portion, and a homologue of RAD9 on the 3′ portion.	scaffold_11:246253-252630		
J	3	54311	N/A	-0.6843	0.4688	Related to adenosylmethionine decarboxylase (EC 4.1.1.50)	scaffold_11:268020-269578		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	3	189824	N/A	-1.5188	1.1444	-	scaffold_12:175968-176894		
J	3	54495	N/A	-1.1829	0.5849	-	scaffold_12:807874-809370		
J	3	213321	N/A	-0.9919	0.6558	Hypothetical ras1 guanine nucleotide exchange factor	scaffold_13:1007327-1010867		
J	3	44054	N/A	-1.1468	0.8057	Rhodopsin-like GPCR superfamily	scaffold_13:266650-272045		
J	3	190616	N/A	-1.2616	0.9341	related to GH family 18 endo-chitinase	scaffold_13:37712-39090		
J	3	213129	N/A	-0.886	0.6202	hypothetical protein with esterase/lipase/thioesterase and transmembrane motifs	scaffold_13:546888-548433		
J	3	213003	N/A	-1.0965	0.5808	-	scaffold_13:56747-57469		
J	3	213546	N/A	-0.8942	0.502	Protein kinase	scaffold_14:452800-456822		
J	3	44512	N/A	-1.4916	0.817	FAD linked oxidase	scaffold_14:525344-526832		
J	3	122133	N/A	-1.057	0.6409	Uridine permease/thiamine transporter/allantoin transport	scaffold_14:602511-604242		
J	3	44385	N/A	-0.7399	0.4783	-	scaffold_14:90129-91514		
J	3	44680	N/A	-1.0532	0.5797	FOG: Zn-finger	scaffold_15:105373-107295		
J	3	50841	N/A	-1.217	0.5738	Hypothetical, AAA ATPase, DNA binding	scaffold_15:214629-216658		
J	3	57252	N/A	-0.6877	0.3878	ABC transporter	scaffold_16:360757-362663		
J	3	57297	N/A	-1.8358	1.3176	Hypothetical Mg2+ transporter protein, CorA-like	scaffold_16:837610-839670		
J	3	193981	N/A	-0.6657	0.4567	Putative pyruvate decarboxylase joined with TPR repeat containing protein	scaffold_18:444350-448762		
J	3	55132	N/A	-1.3531	0.9537	-	scaffold_19:392465-393880		
J	3	205063	N/A	-1.04	0.8179	Cation transporter	scaffold_19:85130-87661		
J	3	206802	N/A	-1.4674	0.9749	Serine/threonine protein kinase	scaffold_2:1388714-1390142		
J	3	37057	N/A	-1.1452	0.5825	Arginase/agmatinase/formiminoglutamase	scaffold_2:1734495-1737128		
J	3	52316	N/A	-0.5391	0.3247	-	scaffold_2:1938901-1940054		
J	3	175357	N/A	-0.8256	0.5499	Sugar transporter superfamily	scaffold_2:1980044-1981759		
J	3	137007	N/A	-0.7369	0.383	-	scaffold_2:2680685-2681560		
J	3	52445	N/A	-1.7049	1.1915	-	scaffold_2:3509541-3510474		
J	3	37502	N/A	-1.1525	0.7776	-	scaffold_2:3546126-3546845		
J	3	119945	N/A	-0.5101	0.2873	-	scaffold_2:3609823-3612066		
J	3	37555	N/A	-0.7592	0.4859	Fungal transcriptional regulatory protein	scaffold_2:3703507-3706530		
J	3	52474	N/A	-0.5645	0.2662	FOG: RRM domain	scaffold_2:3795720-3798221		
J	3	207505	N/A	-0.713	0.4175	(pmrA) Secretory pathway Ca2+-ATPase	scaffold_2:3891073-3894402		
J	3	37636	N/A	-1.4648	0.9021	Uracil-DNA glycosylase	scaffold_2:3972647-3973902		
J	3	173029	N/A	-1.205	0.8713	Fungal transcriptional regulatory protein, N-terminal	scaffold_2:596947-598159		
J	3	173978	N/A	-0.5741	0.362	-	scaffold_2:867475-868888		
J	3	55163	N/A	-0.8063	0.5024	Zn-finger-like, PHD finger	scaffold_20:136232-138231		
J	3	176070	N/A	-1.3429	0.7449	ATP-dependent DNA ligase	scaffold_3:1304768-1305867		
J	3	177287	N/A	-0.8072	0.4274	Predicted protein shares limited amino acid sequence identity with the Saccharomyces cerevisiae URB2 gene product; a nucleolar protein required for normal metabolism of the rRNA primary transcript, proposed to be involved in ribosome biogenesis.	scaffold_3:1973598-1978085		
J	3	47488	N/A	-0.971	0.4942	DEAD/DEAH box helicase	scaffold_3:2044572-2047331		
J	3	208202	N/A	-1.8662	0.8603	-	scaffold_3:2724470-2726570	39	
J	3	177486	N/A	-0.8603	0.4259	Predicted ethanolamine kinase	scaffold_3:2728329-2729840	39	
J	3	176123	N/A	-1.2205	0.7796	-	scaffold_3:2736870-2737247	40	
J	3	198697	N/A	-1.2354	0.7124	Predicted transporter (major facilitator superfamily)	scaffold_3:2738208-2740002	40	
J	3	177340	N/A	-0.7693	0.4239	Metallophosphoesterase	scaffold_3:2746564-2748609		
J	3	208336	N/A	-0.6604	0.4286	Hypothetical. Possible role in carbohydrate metabolism	scaffold_3:3137664-3139790		
J	3	175806	N/A	-0.8822	0.4806	Candidate Cytochrome c oxidase	scaffold_3:3258579-3259184		
J	3	208443	N/A	-0.6191	0.3481	-	scaffold_3:3411705-3414259		
J	3	176655	N/A	-0.9085	0.525	Predicted translation product shares sequence similarity to the Saccharomyces cerevisiae RRN6 gene product; a protein involved in the transcription of 35S rRNA genes by RNA polymerase I; component of the core factor (CF) complex also composed of Rrn11p, Rrn7p and TATA-binding protein.	scaffold_3:3543287-3547070		
J	3	179964	N/A	-0.9455	0.5485	hypothetical ATP-dependent helicase with DEAD/DEAH box domain	scaffold_4:1271962-1276767		
J	3	178677	N/A	-0.7539	0.5285	C2C2-type Zn-finger protein	scaffold_4:1520466-1521521		
J	3	39136	N/A	-1.3267	0.8634	-	scaffold_4:1527513-1527923		
J	3	52996	N/A	-0.7807	0.4906	Related to ubiquinone biosynthesis methyltransferase COQ5 (S. cerevisiae)	scaffold_4:1699132-1700156		
J	3	39215	N/A	-0.7314	0.4311	Ribosomal protein L6	scaffold_4:1748295-1749190		
J	3	179142	N/A	-1.2428	0.8359	Fungal specific transcription factor	scaffold_4:2351564-2354167		
J	3	39399	N/A	-1.053	0.7099	-	scaffold_4:2397047-2397962		
J	3	48109	N/A	-0.8355	0.6054	Myosin class II heavy chain	scaffold_4:2429684-2433338		
J	3	208611	N/A	-1.1067	0.6299	-	scaffold_4:440182-441033		
J	3	38814	N/A	-0.6397	0.4333	-	scaffold_4:454169-456396		
J	3	178237	N/A	-1.0422	0.5886	-	scaffold_4:828499-829634		
J	3	40115	N/A	-1.7431	1.0486	hypothetical protein with four predicted transmembrane domains	scaffold_5:1923039-1924277		
J	3	209439	N/A	-0.9586	0.662	candidate HMG-CoA reductase	scaffold_5:575407-579003		
J	3	126931	N/A	-1.4148	1.1231	Hypothetical glutathione S-transferase	scaffold_5:588619-589470		
J	3	180556	N/A	-0.8204	0.4655	Protein kinase	scaffold_5:836276-839669		
J	3	210021	N/A	-0.8864	0.5109	-	scaffold_6:196246-197446		
J	3	210156	N/A	-1.2802	0.7486	-	scaffold_6:785904-786979		
J	3	40316	N/A	-1.4817	0.9791	AAA ATPase	scaffold_6:95209-96514		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	3	56494	N/A	-0.5744	0.4188	-	scaffold_7:1479046-1479797		
J	3	141246	N/A	-1.8092	1.2242	-	scaffold_7:1727421-1728601		
J	3	200967	N/A	-0.5735	0.2946	-	scaffold_7:400596-401969		
J	3	201684	N/A	-0.5725	0.3786	U1 small nuclear ribonucleoprotein (RRM superfamily)	scaffold_8:1204789-1206176	41	
J	3	53866	N/A	-0.8509	0.6104	Hypothetical G-protein with WD-40 repeat	scaffold_8:1209506-1211588	41	
J	3	185272	N/A	-0.8846	0.5856	-	scaffold_8:1441146-1442621		
J	3	211265	N/A	-0.9886	0.4926	-	scaffold_8:1453152-1454327		
J	3	49445	N/A	-1.0203	0.5743	Hypothetical Peptidase S24, S26A and S26B	scaffold_8:1511614-1512232		
J	3	41556	N/A	-1.1652	0.7193	-	scaffold_8:332278-335172		
J	3	185630	N/A	-0.9727	0.6153	Helicase, C-terminal	scaffold_8:970285-972244		
J	3	54007	N/A	-0.7478	0.4846	Projectin/twitchin and related proteins	scaffold_9:1065914-1067929		
J	3	42089	N/A	-0.8346	0.4629	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae SEN1 gene product; a nuclear protein, putative helicase required for processing of tRNAs, rRNAs, and small nuclear RNAs; potential Cdc28p substrate.	scaffold_9:198687-204911		
J	3	42291	N/A	-1.2793	0.9379	-	scaffold_9:798874-800332		
J	4	172247	N/A	-1.0409	0.9181	related to UDP-N-acetylglucosaminyltransferase [Aspergillus fumigatus Af293]	scaffold_1:2488649-2493762		
J	4	170706	N/A	-0.8217	0.7292	Fungal transcriptional regulatory protein	scaffold_1:260095-262045		
J	4	119363	N/A	-0.8376	0.6694	-	scaffold_1:2893987-2896964		
J	4	36333	N/A	-0.7494	0.6003	Hypothetical protein.	scaffold_1:3303985-3304938		
J	4	170115	N/A	-0.7924	0.6566	Amidase	scaffold_1:3913970-3915704		
J	4	36569	N/A	-1.0025	0.8243	-	scaffold_1:3959424-3963727		
J	4	46333	N/A	-0.8823	0.768	RNA polymerase II transcription initiation factor TFIIA	scaffold_1:591287-593017		
J	4	187061	N/A	-0.8893	0.6104	Putative Mg2+ transporter protein, CorA-like	scaffold_10:292045-293213		
J	4	42698	N/A	-0.6544	0.6241	-	scaffold_10:407275-407753		
J	4	187847	N/A	-0.6782	0.4792	Eukaryotic initiation factor	scaffold_10:487219-487688		
J	4	42764	N/A	-1.2522	1.1518	-	scaffold_10:623048-623841		
J	4	212420	N/A	-0.5063	0.3637	Hypothetical ribosomal protein	scaffold_11:286159-287179		
J	4	50062	N/A	-0.5738	0.5092	Hypothetical TGc (transglutaminase/protease-like) domain-containing protein involved in cytokinesis	scaffold_11:331124-335032		
J	4	212323	N/A	-1.0565	0.7946	This protein is a component of the core form of RNA polymerase transcription factor TFIIH which has both protein kinase and DNA-dependent ATPase/helicase activities and is essential for transcription and nucleotide excision repair;this gene is known as SSL1 in S.cerevisiae	scaffold_11:33757-35275		
J	4	188343	N/A	-0.9222	0.8972	-	scaffold_11:4607-5197		
J	4	54287	N/A	-0.6422	0.5205	Transcriptional repressors of the hairy/E(spl) family (contains HLH)	scaffold_11:82971-83626		
J	4	127917	N/A	-0.7043	0.6713	Peroxisomal membrane protein MPV17 and related proteins	scaffold_12:381624-382425		
J	4	213404	N/A	-0.9378	0.8313	-	scaffold_13:1208219-1208883		
J	4	50490	N/A	-1.0967	0.9209	hypothetical DNA mismatch repair protein	scaffold_13:435659-439525		
J	4	128109	N/A	-1.4009	1.1567	-	scaffold_14:719383-719622		
J	4	136903	N/A	-0.5428	0.5306	hypothetical, some similarity to monooxygenase	scaffold_14:801387-802166		
J	4	50853	N/A	-1.0334	0.835	hypothetical DNA mismatch repair protein MutS, N-terminal	scaffold_15:262800-266291		
J	4	138621	N/A	-0.6577	0.6323	Phosphatidylinositol 4-kinase	scaffold_15:37303-43668		
J	4	192439	N/A	-0.7498	0.619	ATP binding protein	scaffold_16:854557-855285		
J	4	45693	N/A	-0.6432	0.5079	-	scaffold_19:181306-182614		
J	4	36936	N/A	-0.7977	0.6475	-	scaffold_2:1303528-1305475		
J	4	52278	N/A	-0.5172	0.4742	RNA-processing protein	scaffold_2:1691148-1694477		
J	4	174161	N/A	-0.743	0.5503	snRNP A' protein	scaffold_2:1829517-1832399		
J	4	52306	N/A	-0.6486	0.6549	-	scaffold_2:1872994-1875969		
J	4	55590	N/A	-0.8537	0.7397	Phosphoglucomutase (Glucose phosphomutase) (PGM)	scaffold_2:1928550-1930348		
J	4	207025	N/A	-1.1556	1.0214	Hypothetical G-protein with WD-40 repeat	scaffold_2:1940598-1942629		
J	4	207109	N/A	-0.8993	0.9402	-	scaffold_2:2552211-2558471		
J	4	175052	N/A	-0.4822	0.3794	Hypothetical monooxygenase similar to VerA from Aspergillus flavus and Aspergillus nomius	scaffold_2:3098990-3100777		
J	4	207316	N/A	-0.88	0.7547	-	scaffold_2:3279362-3281069		
J	4	37491	N/A	-0.7067	0.6476	Hypothetical heterokaryon incompatibility factor	scaffold_2:3511476-3513708		
J	4	128731	N/A	-1.1508	1.0243	Annexin	scaffold_2:3721589-3727997		
J	4	52472	N/A	-0.8112	0.7095	-	scaffold_2:3789487-3789893		
J	4	36822	N/A	-0.6121	0.4625	Hypothetical regulatory subunit of the 20S preoteasome	scaffold_2:892497-893550		
J	4	38018	N/A	-0.7473	0.6223	-	scaffold_3:1155086-1159368		
J	4	175996	N/A	-1.4021	1.1284	Cytochrome P450	scaffold_3:1966044-1967630		
J	4	175686	N/A	-0.9738	0.9454	Myosin class II heavy chain	scaffold_3:2959111-2962475		
J	4	119822	N/A	-0.8622	0.7206	Nucleolar GTPase/ATPase p130	scaffold_3:3034061-3036762		
J	4	38576	N/A	-0.7089	0.6736	-	scaffold_3:3302461-3303757		
J	4	52525	N/A	-1.1467	1.0504	Aminotransferase, class-II	scaffold_3:405123-406941		
J	4	37812	N/A	-0.5353	0.4083	hypothetical Aflatoxin biosynthesis regulatory protein	scaffold_3:491597-492920		
J	4	37856	N/A	-0.8206	0.7667	Alkyl hydroperoxide reductase/peroxiredoxin	scaffold_3:659088-659938	42	
J	4	37857	N/A	-0.7856	0.6262	Heat shock transcription factor	scaffold_3:663138-665599	42	
J	4	119479	N/A	-0.9844	0.9039	DEAD/DEAH box helicase	scaffold_3:901915-904099		
J	4	207764	N/A	-0.4497	0.4044	G/T mismatch-specific thymine DNA glycosylase	scaffold_3:913156-915451		
J	4	52853	N/A	-0.5854	0.5445	Non-ribosomal peptide synthetase	scaffold_4:119094-120625		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	4	39356	N/A	-0.742	0.6371	-	scaffold_4:2251581-2253163		
J	4	178195	N/A	-0.6835	0.5923	hypothetical protein with an ARM repeat fold	scaffold_4:2383370-2388913		
J	4	52868	N/A	-0.549	0.4214	Hypothetical protein transporter of the TRAM (translocating chain-associating membrane) super-family	scaffold_4:301901-303365		
J	4	52883	N/A	-0.698	0.5854	Hypothetical subunit of the 20S proteasome	scaffold_4:460726-462011		
J	4	53266	N/A	-0.6815	0.6437	-	scaffold_5:1237591-1239602		
J	4	209656	N/A	-1.0116	0.8652	-	scaffold_5:1339512-1340960		
J	4	180472	N/A	-0.4545	0.4331	WD40 repeat-containing protein	scaffold_5:1531620-1533668		
J	4	136845	N/A	-0.6363	0.4676	Ribosomal protein	scaffold_5:1655111-1655620		
J	4	180563	N/A	-1.4696	1.2009	-	scaffold_5:1926608-1927935		
J	4	40173	N/A	-0.7127	0.5088	Small nuclear ribonucleoprotein	scaffold_5:2115232-2115647		
J	4	39638	N/A	-0.7395	0.5854	Autophagy protein Apg5	scaffold_5:254265-255341		
J	4	39673	N/A	-0.7925	0.7321	Nucleolar GTPase/ATPase p130	scaffold_5:368245-372330	43	
J	4	199857	N/A	-0.8664	0.7277	-	scaffold_5:373319-374375	43	
J	4	39724	N/A	-0.743	0.5911	Hypothetical. Sequence homology with S. cerevisiae SKI6; 3'-to-5' phosphorolytic exoribonuclease. Subunit of the exosome; required for 3' processing of the 5.8S rRNA; involved in 3' to 5' mRNA degradation and translation inhibition of non-poly(A) mRNAs.	scaffold_5:563767-564647		
J	4	136085	N/A	-0.6713	0.5561	-	scaffold_5:664480-665160		
J	4	39772	N/A	-0.7921	0.7541	Kinesin-like protein	scaffold_5:738182-741272		
J	4	182673	N/A	-1.4406	1.2994	-	scaffold_6:1222820-1224098		
J	4	209988	N/A	-0.546	0.4481	-	scaffold_6:151265-155842		
J	4	40780	N/A	-0.7319	0.6413	-	scaffold_6:1629260-1630833		
J	4	182442	N/A	-0.661	0.5834	-	scaffold_6:24022-26998		
J	4	48737	N/A	-0.8418	0.6799	Protein kinase	scaffold_6:912265-915412		
J	4	40555	N/A	-0.5965	0.4684	Related to NADH-ubiquinone oxidoreductase	scaffold_6:924141-924580		
J	4	40569	N/A	-0.6427	0.6061	ATPases associated with various cellular activities (AAA)	scaffold_6:963332-965134		
J	4	56472	N/A	-0.8784	0.7536	-	scaffold_7:1152999-1154330		
J	4	210464	N/A	-1.0124	0.7945	-	scaffold_7:329575-330501		
J	4	48946	N/A	-0.9136	0.7638	-	scaffold_7:345058-346158		
J	4	41168	N/A	-0.791	0.6641	Flavin-containing monooxygenase	scaffold_7:857219-858842		
J	4	184862	N/A	-0.8975	0.5355	Hypothetical Cl- channel, voltage gated	scaffold_8:1022422-1025320		
J	4	49209	N/A	-0.8777	0.7387	Actin/actin-like	scaffold_8:111291-112907		
J	4	120986	N/A	-0.5632	0.467	Fungal specific transcription factor	scaffold_8:1373752-1375676		
J	4	49427	N/A	-0.8379	0.8227	-	scaffold_8:1401888-1403848		
J	4	185082	N/A	-0.7154	0.5444	Fungal transcriptional regulatory protein	scaffold_8:1680497-1681936		
J	4	201912	N/A	-0.909	0.8062	-	scaffold_9:365901-366785		
J	4	42149	N/A	-0.6485	0.5594	-	scaffold_9:402066-402611		
J	4	211472	N/A	-1.4004	1.2443	Protein kinase	scaffold_9:440540-442612		
J	4	201966	N/A	-0.6928	0.5642	Hypothetical NADH:ubiquinone oxidoreductase	scaffold_9:488803-489267		
J	4	186833	N/A	-1.1001	0.8033	UBA/THIF-type NAD/FAD binding fold	scaffold_9:895989-897396		
J	5	46416	N/A	-0.7268	0.5488	Predicted heme/steroid binding protein	scaffold_1:1090553-1091381		
J	5	35759	N/A	-0.5548	0.5754	-	scaffold_1:1268330-1269796		
J	5	205368	N/A	-0.7364	0.6547	Peptidase	scaffold_1:149038-150612		
J	5	35897	N/A	-0.6793	0.4374	COP9 signalosome, subunit CSN7	scaffold_1:1698069-1699078		
J	5	35899	N/A	-0.8629	0.6574	hypothetical protein; KOG Class: Chromatin structure and dynamics;	scaffold_1:1704709-1705887		
J	5	170758	N/A	-0.9311	0.6133	-	scaffold_1:1896194-1898946		
J	5	36015	N/A	-0.6635	0.7282	-	scaffold_1:2037843-2039253		
J	5	36134	N/A	-0.5595	0.5547	Myosin regulatory light chain	scaffold_1:2416174-2416797		
J	5	171196	N/A	-0.8838	0.8997	-	scaffold_1:2450819-2452335		
J	5	46685	N/A	-1.1248	1.0105	-	scaffold_1:2532387-2533934		
J	5	46716	N/A	-0.8083	0.6378	-	scaffold_1:2914491-2915673		
J	5	51997	N/A	-0.5611	0.6205	(xyrA) D-xylose reductase xyrA whose expression requires the xylanolytic transcriptional activator XlnR; involved in pentose and glucuronate interconversions	scaffold_1:2935164-2936245		
J	5	124929	N/A	-0.6233	0.4531	Metallophosphoesterase	scaffold_1:3076632-3077630		
J	5	46834	N/A	-0.5926	0.4942	Major facilitator superfamily	scaffold_1:3601249-3602675		
J	5	54079	N/A	-1.6083	1.2615	-	scaffold_10:159741-161033		
J	5	187626	N/A	-0.5205	0.4083	-	scaffold_10:1899987-1900641		
J	5	126897	N/A	-0.7145	0.472	Tyrosine specific protein phosphatase and dual specificity protein phosphatase	scaffold_10:1913032-1913750		
J	5	42846	N/A	-0.639	0.5046	-	scaffold_10:930663-932198		
J	5	188323	N/A	-0.5921	0.4738	Fungal specific transcription factor	scaffold_11:1571115-1573635		
J	5	188502	N/A	-0.8246	0.6604	Polyketide synthase	scaffold_11:469575-471049		
J	5	189528	N/A	-1.0909	0.9224	-	scaffold_12:1049345-1050517		
J	5	189430	N/A	-0.5375	0.4366	Hypothetical 2-nitropropane dioxygenase. (EC 1.13.11.32)	scaffold_12:1063124-1064191		
J	5	190098	N/A	-0.5518	0.4945	Fungal transcriptional regulatory protein	scaffold_12:896429-898081		
J	5	57113	N/A	-0.4016	0.3764	Longevity-assurance protein (LAG1)	scaffold_13:1090256-1091816		
J	5	213612	N/A	-0.9612	0.9661	Nucleolar GTPase	scaffold_14:916678-918442		
J	5	213647	N/A	-0.7592	0.7096	Kinesin-like protein	scaffold_15:22029-24943		
J	5	191996	N/A	-0.8912	0.7737	Hypothetical flavin-containing amine oxidase	scaffold_15:826216-827711		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	5	134242	N/A	-0.9781	0.8365	-	scaffold_16:105461-106754		
J	5	204464	N/A	-0.9945	0.7845	Hypothetical protein. Contains a putative BAR domain.	scaffold_16:646207-647739		
J	5	45365	N/A	-0.4336	0.448	hypothetical 3-oxo-5-alpha-steroid 4-dehydrogenase	scaffold_17:393931-395035		
J	5	214568	N/A	-1.0871	0.9278	Extracellular protein SEL-1 and related proteins	scaffold_18:494808-496306		
J	5	194262	N/A	-1.0921	0.847	Esterase/lipase/thioesterase	scaffold_19:178038-179111		
J	5	120936	N/A	-0.5434	0.4656	Fungal transcriptional regulatory protein	scaffold_19:373547-375698		
J	5	205156	N/A	-0.7417	0.5414	GMC oxidoreductase	scaffold_19:578673-580277		
J	5	52229	N/A	-1.2816	0.9961	Zinc-containing alcohol dehydrogenase	scaffold_2:1332156-1336712		
J	5	37083	N/A	-1.1577	0.8655	-	scaffold_2:1816002-1816689		
J	5	197516	N/A	-0.7355	0.5979	Predicted translation product shares amino acid sequence similarity to the Saccharomyces cerevisiae REX2 gene product; an RNA exonuclease, required for U4 snRNA maturation; functions redundantly with Rnh70p in 5.8S rRNA maturation, and with Rnh70p and Rex3p in processing of U5 snRNA and RNase P RNA (yeast); member of RNase D family of exonucleases.	scaffold_2:1924890-1928044		
J	5	207032	N/A	-1.0667	1.0284	-	scaffold_2:1955675-1957161		
J	5	55598	N/A	-0.6686	0.4596	-	scaffold_2:2510496-2511991		
J	5	55605	N/A	-0.6975	0.69	Actin/actin-like	scaffold_2:2646664-2648322		
J	5	207212	N/A	-1.0033	0.7578	Hypothetical MCM5	scaffold_2:2933921-2936269		
J	5	36675	N/A	-0.2883	0.3002	Predicted phosphate acyltransferase	scaffold_2:336340-337498		
J	5	137850	N/A	-0.5699	0.4272	-	scaffold_2:3756240-3756789		
J	5	46942	N/A	-0.3214	0.3223	AAA ATPase	scaffold_2:799739-802014		
J	5	194896	N/A	-0.5687	0.4194	hypothetical amine oxidase	scaffold_21:204517-206360		
J	5	214881	N/A	-0.6382	0.5288	Short-chain dehydrogenase/reductase	scaffold_24:100919-101942		
J	5	38094	N/A	-0.8695	0.7819	hypothetical protein with predicted histone-fold	scaffold_3:1549113-1549997		
J	5	47410	N/A	-0.4484	0.4536	hypothetical protein with predicted fungal transcriptional regulatory domain	scaffold_3:1601472-1603254		
J	5	47416	N/A	-0.5668	0.468	Hypothetical protein, contains DENN domain	scaffold_3:1645420-1648367		
J	5	142108	N/A	-1.5615	1.374	-	scaffold_3:1753026-1753957		
J	5	124591	N/A	-0.4285	0.4541	Thioesterase superfamily	scaffold_3:2899206-2899928		
J	5	38577	N/A	-1.1158	0.9332	Protein kinase	scaffold_3:3304599-3306018		
J	5	47739	N/A	-0.6254	0.5608	Cell cycle-associated protein Mob1-1	scaffold_3:3463738-3464721		
J	5	208837	N/A	-0.7921	0.5907	Aromatic-ring hydroxylase	scaffold_4:1378195-1379627		
J	5	39391	N/A	-0.8338	0.6607	-	scaffold_4:2374088-2374997		
J	5	53049	N/A	-0.6428	0.5861	Ras-related small GTPase, Rho type	scaffold_4:2470322-2471315		
J	5	178411	N/A	-0.4792	0.4413	-	scaffold_4:2590399-2591245		
J	5	38788	N/A	-0.8333	0.5479	Amino acid/polyamine transporter	scaffold_4:360246-362397		
J	5	199085	N/A	-0.7776	0.6079	putative GH family 16 GPI-glucanosyltransferase	scaffold_4:414105-415276		
J	5	38818	N/A	-0.8051	0.7848	Ras GTPase	scaffold_4:467880-468829		
J	5	209757	N/A	-0.8299	0.7404	-	scaffold_5:1710997-1712712		
J	5	199928	N/A	-0.9011	0.8787	Predicted hydrolase	scaffold_5:605862-607177		
J	5	209244	N/A	-0.4285	0.4887	Oxidoreductase	scaffold_5:73272-74671		
J	5	48869	N/A	-0.5921	0.4376	-	scaffold_6:1735047-1735766		
J	5	182862	N/A	-0.5212	0.4629	Zinc-containing alcohol dehydrogenase	scaffold_6:1973035-1974147		
J	5	56311	N/A	-1.1884	1.172	hypothetical Glucose-methanol-choline oxidoreductase	scaffold_6:691821-693761		
J	5	40558	N/A	-0.5663	0.5093	Hypothetical transcription initiation factor TFIID, subunit TAF7	scaffold_6:928162-929643		
J	5	41279	N/A	-0.5121	0.3615	-	scaffold_7:1285697-1287644		
J	5	210724	N/A	-1.4197	0.988	GABA/amino acid permease	scaffold_7:1353282-1355857		
J	5	125933	N/A	-1.2668	0.8888	Aldo/keto reductase family proteins	scaffold_7:1414314-1415334		
J	5	184284	N/A	-0.6842	0.5886	Serine/threonine protein kinase	scaffold_7:303575-305009		
J	5	210479	N/A	-0.786	0.636	Hypothetical MCM7	scaffold_7:350163-352749		
J	5	183201	N/A	-0.9116	0.8772	-	scaffold_7:682053-688273		
J	5	41197	N/A	-0.9166	0.79	-	scaffold_7:933264-936509		
J	5	41557	N/A	-0.6783	0.5914	Hypothetical arginase (EC 3.5.3.1)	scaffold_8:336026-336916		
J	5	46177	N/A	-0.6839	0.5414	-	scaffold_88:185-1014		
J	5	186367	N/A	-0.5115	0.409	U4/U6 small nuclear ribonucleoprotein Prp4 (contains WD40 repeats)	scaffold_9:1363944-1365617		
J	5	56736	N/A	-1.0009	0.8586	Haloacid dehalogenase-like hydrolase	scaffold_9:1572490-1573296		
J	5	211385	N/A	-1.1495	0.9103	-	scaffold_9:214244-216516		
J	5	49550	N/A	-0.6313	0.49	Hypothetical protein with BRCT domain	scaffold_9:403118-404499		
J	6	35715	N/A	-0.5248	0.5469	-	scaffold_1:1124175-1125800		
J	6	171843	N/A	-0.2901	0.3011	-	scaffold_1:1394902-1395826	44	
J	6	172707	N/A	-0.9282	0.6898	protease	scaffold_1:1395934-1396938	44	
J	6	205755	N/A	-0.8193	0.6584	emp24/gp25L/p24 family of membrane trafficking proteins	scaffold_1:1517042-1518017		
J	6	51865	N/A	-0.5774	0.4741	SAM (and some other nucleotide) binding motif	scaffold_1:1666685-1667884		
J	6	46605	N/A	-0.7466	0.6711	-	scaffold_1:2077024-2079974		
J	6	55234	N/A	-0.9484	0.6883	Hypothetical CDP-alcohol phosphatidyltransferase	scaffold_1:231471-232441		
J	6	170726	N/A	-0.692	0.5357	-	scaffold_1:2937469-2942278		
J	6	170577	N/A	-0.6944	0.5639	Hypothetical protein with TPR-like domain	scaffold_1:2967707-2969276		
J	6	119312	N/A	-0.4664	0.4939	Extracellular protein SEL-1 and related proteins	scaffold_1:603375-606688		
J	6	205507	N/A	-0.7453	0.6557	-	scaffold_1:628150-631529		
J	6	35600	N/A	-0.9645	0.6254	-	scaffold_1:801958-802605		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	6	120185	N/A	-0.8991	0.5922	Hypothetical protein. May be a transcription factor due to a Zn-finger domain.	scaffold_10:1784965-1787258		
J	6	43028	N/A	-0.793	0.6184	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 2510; KOG Description: SWI-SNF chromatin-remodeling complex protein	scaffold_10:1916442-1917377	45	
J	6	43031	N/A	-0.8273	0.7472	-	scaffold_10:1921308-1921781	45	
J	6	187212	N/A	-0.6485	0.5124	-	scaffold_10:316203-318245		
J	6	54108	N/A	-0.8296	0.753	Zn-finger-like, PHD finger	scaffold_10:439886-441241		
J	6	211899	N/A	-0.7012	0.7697	Protein kinase	scaffold_10:630401-640287		
J	6	187609	N/A	-0.6312	0.5293	This protein does not have homology with proteins with confirmed asparginase activity	scaffold_10:731736-733426		
J	6	43389	N/A	-0.5445	0.4502	-	scaffold_11:1111695-1113197		
J	6	43469	N/A	-1.6178	1.2789	Actin-binding, actinin-type	scaffold_11:1360101-1361599		
J	6	119587	N/A	-0.6823	0.477	Glycosyl hydrolases family 18	scaffold_11:189241-192922		
J	6	188478	N/A	-0.7241	0.5229	-	scaffold_11:198093-198794		
J	6	188704	N/A	-0.6334	0.4345	Hypothetical signal peptidase. Signalp predictions suggests that it is anchored to a membrane.	scaffold_11:412595-413567		
J	6	188902	N/A	-0.7416	0.6549	-	scaffold_11:474751-476662		
J	6	43224	N/A	-1.0916	1.0103	Fungal transcriptional regulatory protein	scaffold_11:540939-542684		
J	6	189790	N/A	-0.6078	0.554	-	scaffold_12:1002315-1002935		
J	6	43621	N/A	-0.8379	0.4547	SAM (and some other nucleotide) binding motif	scaffold_12:138975-140640		
J	6	43641	N/A	-1.0781	0.955	-	scaffold_12:195218-197460		
J	6	189874	N/A	-0.6011	0.4837	Short-chain dehydrogenase/reductase	scaffold_12:649933-650920		
J	6	50452	N/A	-1.0595	0.9999	-	scaffold_13:229021-229680		
J	6	54582	N/A	-0.7822	0.5701	Ras GTPase	scaffold_13:563583-564529		
J	6	213255	N/A	-0.9947	0.8972	Zn-finger, C2H2 type	scaffold_13:819750-821781		
J	6	190481	N/A	-0.891	0.6152	AMP-dependent synthetase and ligase	scaffold_13:861005-862772		
J	6	54635	N/A	-0.8838	0.8013	-	scaffold_13:890217-891658		
J	6	191589	N/A	-0.8642	0.9049	-	scaffold_14:373259-374315		
J	6	191266	N/A	-0.8924	0.6886	Fungal transcriptional regulatory protein	scaffold_14:675901-678680		
J	6	137560	N/A	-0.4111	0.3856	-	scaffold_14:813692-814097		
J	6	50856	N/A	-0.8781	0.5884	Hypothetical dehydrogenase. Shows homology to alcohol dehydrogenase (Pseudomonase fluorescens) and NADP-dependent leukotriene b4 12-hydroxydehydrogenase (Botryotinia fuckeliana)	scaffold_15:276439-277559		
J	6	213827	N/A	-0.9065	0.6457	Permease of the major facilitator superfamily	scaffold_15:853701-855322		
J	6	45057	N/A	-0.4645	0.4071	-	scaffold_16:317612-317924		
J	6	192619	N/A	-0.5438	0.366	Serine carboxypeptidase	scaffold_16:498881-500827		
J	6	57291	N/A	-0.8105	0.7993	Serine/threonine protein kinase	scaffold_16:791876-793506		
J	6	45757	N/A	-0.3958	0.3519	-	scaffold_19:371710-372117		
J	6	120519	N/A	-0.9745	0.8444	-	scaffold_19:414187-416285		
J	6	214632	N/A	-0.6384	0.4543	candidate acetyltransferase	scaffold_19:51339-52280		
J	6	206713	N/A	-0.7296	0.6502	-	scaffold_2:1080123-1081780	46	
J	6	175122	N/A	-0.8562	0.7518	-	scaffold_2:1084086-1084903	46	
J	6	206715	N/A	-0.5139	0.4266	putative calcium-dependent, mannose-binding lectin implicated in substrate-specific glycoprotein secreting pathway	scaffold_2:1106935-1108180		
J	6	206787	N/A	-0.9804	0.9658	Sec1-like protein	scaffold_2:1344284-1346689		
J	6	52243	N/A	-1.0962	1.2079	Uncharacterized conserved protein	scaffold_2:1444237-1453884		
J	6	172938	N/A	-0.947	0.7534	-	scaffold_2:2685766-2686812		
J	6	173077	N/A	-0.347	0.35	Dephospho-CoA kinase	scaffold_2:3146374-3147201		
J	6	126865	N/A	-0.4523	0.3941	hypothetical protein with predicted transcription factor and histone-fold; KOG Class: Transcription; KOG Id: 1659; KOG description: Class 2 transcription repressor NC2, α subunit (DRAP1)	scaffold_2:323961-324921		
J	6	137430	N/A	-0.9437	0.6459	-	scaffold_2:3531448-3531911		
J	6	174693	N/A	-0.4865	0.4694	-	scaffold_2:3913966-3916566		
J	6	52135	N/A	-0.3688	0.4464	Related to DNA-directed RNA polymerase	scaffold_2:487531-488797		
J	6	206541	N/A	-0.6384	0.4807	Hypothetical protein with RING finger domain	scaffold_2:563138-564673	47	
J	6	173346	N/A	-0.6082	0.7612	DEAD/DEAH box helicase	scaffold_2:569194-576170	47	
J	6	36749	N/A	-0.6561	0.4903	Collagens (type IV and type XIII), and related proteins	scaffold_2:622716-625229		
J	6	36787	N/A	-0.5163	0.4841	-	scaffold_2:774535-775480	48	
J	6	173999	N/A	-0.8547	0.8714	SMC protein	scaffold_2:777571-781388	48	
J	6	51412	N/A	-0.7612	0.6017	-	scaffold_20:113428-113974		
J	6	45893	N/A	-0.3389	0.299	Putative glucosyltransferase	scaffold_20:172895-174710		
J	6	45910	N/A	-0.9378	0.8623	Related to Deoxyribodipyrimidine photo-lyase (DNA photolyase)	scaffold_20:231855-233669		
J	6	127816	N/A	-0.7706	0.5811	SNARE protein	scaffold_20:256615-257387		
J	6	144225	N/A	-0.8006	0.8121	-	scaffold_256:403-1185		
J	6	38046	N/A	-0.6619	0.563	Inner centromere protein	scaffold_3:1271934-1276043		
J	6	47380	N/A	-0.6278	0.4943	NRPS	scaffold_3:1292122-1294908		
J	6	38101	N/A	-0.3814	0.367	Tyrosine protein kinase	scaffold_3:1563550-1571801		
J	6	198372	N/A	-0.7269	0.635	Hypothetical exocyst complex subunit	scaffold_3:1695731-1697938		
J	6	207921	N/A	-0.3737	0.3921	H4 - histone 4 protein	scaffold_3:1792947-1793420		
J	6	47522	N/A	-0.9305	1.0168	HLH transcription factor EBF/Olf-1 and related DNA binding proteins	scaffold_3:2194417-2198835		
J	6	47528	N/A	-0.5118	0.5157	Notchless-like WD40 repeat-containing protein	scaffold_3:2233535-2234901		
J	6	52717	N/A	-0.9632	0.8918	Shares limited amino acid sequence identity with ribosomal protein L15, bacterial form.	scaffold_3:2600355-2601405		
J	6	138318	N/A	-0.56	0.4885	-	scaffold_3:2733467-2733766		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	6	121206	N/A	-0.6674	0.5491	Prolyl-tRNA synthetase	scaffold_3:2932383-2934405		
J	6	47276	N/A	-0.9343	0.7177	RNA-binding nuclear protein (MAK16) containing a distinct C4 Zn-finger	scaffold_3:602642-604021		
J	6	52941	N/A	-1.0669	0.9967	-	scaffold_4:1016641-1018184		
J	6	208803	N/A	-0.7621	0.6737	Uncharacterized conserved protein, contains BSD domain	scaffold_4:1239875-1241228		
J	6	178469	N/A	-1.0204	1.1618	Uncharacterized conserved protein Sand	scaffold_4:1287735-1289911		
J	6	124897	N/A	-0.5572	0.4602	Golgi reassembly stacking protein GRASP65, contains PDZ domain	scaffold_4:1491953-1493107		
J	6	39360	N/A	-1.0498	1.0517	Zinc-binding oxidoreductase	scaffold_4:2265584-2266747		
J	6	199051	N/A	-0.8572	0.8402	Sugar transporter superfamily	scaffold_4:228479-231215		
J	6	38774	N/A	-0.6527	0.4111	Amidohydrolase-like	scaffold_4:316845-318212	49	
J	6	179491	N/A	-1.4093	0.8767	Serine/threonine protein kinase	scaffold_4:318727-320841	49	
J	6	208691	N/A	-1.0545	0.6304	Major facilitator superfamily	scaffold_4:728981-730735		
J	6	121905	N/A	-0.914	0.8613	Smr protein/MutS2 C-terminal	scaffold_4:738756-740336		
J	6	180458	N/A	-0.6071	0.3768	Acetamidase/Formamidase	scaffold_5:1136985-1138482		
J	6	53283	N/A	-0.8809	0.9503	Zn-finger-like, PHD finger	scaffold_5:1421642-1423713		
J	6	56222	N/A	-0.7896	0.6385	-	scaffold_5:1597197-1600182		
J	6	209800	N/A	-0.8604	0.6903	Hypothetical U2 snRNP auxilliary factor, large subunit, splicing factor	scaffold_5:1795509-1797556		
J	6	40100	N/A	-0.5433	0.4192	Hypothetical AAA ATPase	scaffold_5:1854408-1857321		
J	6	142488	N/A	-0.6499	0.3907	Basic-leucine zipper (bZIP) transcription factor	scaffold_5:407590-409084		
J	6	56150	N/A	-0.8305	0.6913	Cyclin B and related kinase-activating proteins	scaffold_5:514503-515759		
J	6	180989	N/A	-0.7911	0.6617	Hypothetical spliceosome subunit	scaffold_5:784103-791161		
J	6	48357	N/A	-0.3924	0.3422	-	scaffold_5:845624-847006		
J	6	53240	N/A	-0.837	0.8383	Lipocalin-related protein	scaffold_5:975513-976765		
J	6	48772	N/A	-1.0187	0.8909	Protein kinase	scaffold_6:1163953-1167554		
J	6	53512	N/A	-1.0192	0.8052	Hypothetical 3′ exoribonuclease	scaffold_6:1589625-1590657		
J	6	40874	N/A	-0.5243	0.4613	-	scaffold_6:1942171-1944396		
J	6	56296	N/A	-0.9382	0.7742	-	scaffold_6:459758-460206		
J	6	40408	N/A	-0.9954	0.8471	-	scaffold_6:476676-477579		
J	6	183075	N/A	-0.3707	0.3896	-	scaffold_6:532818-536930		
J	6	183104	N/A	-0.9215	0.5482	putative chromosome condensation protein	scaffold_6:728256-729380		
J	6	40936	N/A	-0.3527	0.3537	Myb, DNA-binding	scaffold_7:127331-129041		
J	6	184104	N/A	-0.6819	0.425	-	scaffold_7:445161-446519		
J	6	184046	N/A	-0.7564	0.6751	PHD Zn-finger protein	scaffold_7:518822-520222		
J	6	56589	N/A	-0.6807	0.5975	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_8:1035212-1036938		
J	6	184609	N/A	-0.7457	0.6213	Fungal transcriptional regulatory protein, N-terminal	scaffold_8:1148785-1152242		
J	6	211207	N/A	-0.6891	0.5927	-	scaffold_8:1200996-1202465		
J	6	41862	N/A	-0.8814	0.5314	-	scaffold_8:1234319-1235273		
J	6	41882	N/A	-1.0135	0.9218	-	scaffold_8:1300731-1301741		
J	6	49435	N/A	-0.8821	0.7433	-	scaffold_8:1438732-1439448		
J	6	41521	N/A	-0.2881	0.2482	-	scaffold_8:225925-227748		
J	6	49282	N/A	-0.7065	0.4672	SAM-dependent methyltransferases	scaffold_8:514318-515118		
J	6	41667	N/A	-0.8978	0.7621	-	scaffold_8:638074-639862		
J	6	186167	N/A	-0.5191	0.5031	-	scaffold_9:1095038-1098766		
J	6	211598	N/A	-0.5347	0.381	-	scaffold_9:1144226-1147068		
J	6	54015	N/A	-0.6282	0.5908	hypothetical cation transport ATPase	scaffold_9:1172203-1176393		
J	6	56722	N/A	-0.9541	0.7104	-	scaffold_9:1312306-1314275		
J	6	186631	N/A	-1.375	1.1298	-	scaffold_9:1609685-1610398		
J	7	51782	N/A	-0.7803	0.7429	Hypothetical protein kinase	scaffold_1:1009039-1010981		
J	7	170609	N/A	-1.3306	1.2877	-	scaffold_1:1192072-1192732		
J	7	46489	N/A	-0.9087	0.8076	-	scaffold_1:1483353-1484117		
J	7	35896	N/A	-0.8003	0.6955	Regulator of G protein	scaffold_1:1696108-1697339		
J	7	55364	N/A	-0.9302	0.8861	Molecular chaperone Prefoldin	scaffold_1:1807357-1807874		
J	7	172838	N/A	-0.8755	0.8478	Homologue of S. cerevisiae DIS3 gene product, a nucleolar exosome component, involved in rRNA processing and RNA degradation, binds Gsp1p/Ran and enhances the GEF activity of Srm1p, implicated in mitotic control, homologous to the E. coli RNase R of the RNase II family.	scaffold_1:1847263-1850416		
J	7	35984	N/A	-0.9659	0.9559	Peptidase M14, carboxypeptidase A	scaffold_1:1948869-1951066		
J	7	35429	N/A	-1.1706	1.0931	-	scaffold_1:209260-211915		
J	7	206238	N/A	-0.8237	0.8401	Na+/dicarboxylate	scaffold_1:3087100-3089993		
J	7	196801	N/A	-0.6734	0.6889	Seems like two proteins have been combined in one model	scaffold_1:3249531-3251502		
J	7	170268	N/A	-0.8078	0.7487	Iron-containing alcohol dehydrogenase	scaffold_1:3332197-3335761		
J	7	35485	N/A	-0.874	0.8367	Related to saccharopine dehydrogenase (EC 1.5.1.10) from Magnaporthe grisea	scaffold_1:377809-379197		
J	7	46882	N/A	-1.2998	1.1781	Metallophosphoesterase	scaffold_1:3917871-3919823		
J	7	46390	N/A	-1.0652	1.0483	-	scaffold_1:938727-939548		
J	7	186933	N/A	-1.0086	1.0072	Inositol polyphosphate kinase	scaffold_10:1080520-1081988		
J	7	42900	N/A	-0.8412	0.7459	Hypothetical mRNA cleavage and polyadenylation factor IA/II complex subunit	scaffold_10:1093300-1095136		
J	7	54199	N/A	-1.1359	1.1237	-	scaffold_10:1177456-1184184		
J	7	187359	N/A	-0.7836	0.7233	Hypothetical methionyl-tRNA formyltransferase (EC 2.1.2.9)	scaffold_10:1820210-1821572		
J	7	42844	N/A	-0.8768	0.7689	-	scaffold_10:922861-923784		
J	7	212646	N/A	-0.6855	0.6333	-	scaffold_11:1089361-1092643		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	7	129183	N/A	-0.6466	0.6794	Oxidosqualene-lanosterol cyclase and related proteins	scaffold_11:158275-161808		
J	7	188885	N/A	-0.6189	0.5919	Hypothetical protein with DnaJ domain	scaffold_11:477185-479646		
J	7	188714	N/A	-1.0734	0.9512	-	scaffold_11:654906-656042		
J	7	56985	N/A	-0.9653	0.8392	-	scaffold_12:214634-219574		
J	7	43728	N/A	-1.0253	0.9836	Hypothetical mannosyltransferase	scaffold_12:499509-500909		
J	7	121294	N/A	-1.367	1.4153	PHD Zn-finger protein	scaffold_12:514925-516710		
J	7	212997	N/A	-1.0507	0.9401	-	scaffold_13:24883-27576		
J	7	190369	N/A	-0.9239	0.8222	TatD-related DNase	scaffold_13:848989-850113		
J	7	191221	N/A	-0.7931	0.7775	Clathrin adaptor complex	scaffold_14:257464-258862		
J	7	54759	N/A	-1.0244	0.9444	Regulator of Rac1, required for phagocytosis and cell migration	scaffold_14:948944-951214		
J	7	213629	N/A	-0.9455	0.9527	Drebrins and related actin binding proteins	scaffold_14:961220-963798		
J	7	126602	N/A	-0.9266	0.8428	Acyl-CoA:diacylglycerol acyltransferase	scaffold_15:19778-20587		
J	7	192367	N/A	-0.8592	0.7579	Uncharacterized conserved protein, contains TBC domain	scaffold_15:281416-282966		
J	7	192940	N/A	-0.8589	0.7268	-	scaffold_16:636789-638827		
J	7	57296	N/A	-0.7173	0.6199	Nuclear protein ES2	scaffold_16:833005-834438		
J	7	213855	N/A	-0.7656	0.663	DEAD/DEAH box helicase	scaffold_16:84579-86360		
J	7	193079	N/A	-0.6088	0.5763	-	scaffold_16:864868-868057		
J	7	193912	N/A	-0.9882	0.9833	-	scaffold_18:472813-473863		
J	7	205031	N/A	-0.965	0.8852	-	scaffold_18:602509-603671		
J	7	52200	N/A	-0.9057	0.9581	Putative Zinc transporter ZIP, Zn /Fe	scaffold_2:1067376-1068719		
J	7	52210	N/A	-0.8246	0.9356	-	scaffold_2:1178256-1178760		
J	7	46990	N/A	-0.7697	0.7542	-	scaffold_2:1420445-1421431		
J	7	197907	N/A	-0.9968	0.9714	SNARE protein	scaffold_2:3520079-3521251		
J	7	174835	N/A	-1.2616	1.205	Single-stranded DNA-binding replication protein A (RPA), large (70 kD) subunit and related ssDNA-binding proteins	scaffold_2:4015887-4017890		
J	7	52163	N/A	-0.8114	0.7783	Actin/actin-like	scaffold_2:751656-754033		
J	7	194814	N/A	-0.7556	0.717	-	scaffold_20:86993-87632		
J	7	51512	N/A	-1.2123	1.1767	Cytochrome P450	scaffold_22:89766-91425		
J	7	38122	N/A	-0.7505	0.7962	Hypothetical protein kinase	scaffold_3:1635615-1640581		
J	7	207896	N/A	-1.0358	1.0308	Hypothetical small subunit of the clathrin adaptor complex	scaffold_3:1734150-1734893		
J	7	38202	N/A	-1.0367	0.9165	Gamma tubulin	scaffold_3:1914896-1916826		
J	7	208006	N/A	-0.6523	0.6004	Fungal G-protein, α subunit	scaffold_3:1997323-1998575		
J	7	38463	N/A	-0.8883	0.8636	-	scaffold_3:2914182-2917591		
J	7	208421	N/A	-0.8421	0.7664	Ubiquitin protein ligase	scaffold_3:3388997-3392052		
J	7	119526	N/A	-0.7404	0.7568	Kinesin, motor region	scaffold_3:505585-508471		
J	7	37842	N/A	-0.519	0.4999	GTPase-activating protein	scaffold_3:606578-610172		
J	7	178441	N/A	-1.2993	1.1485	Nucleolar GTPase/ATPase p130	scaffold_4:1241539-1243524		
J	7	208820	N/A	-0.9162	0.8723	Predicted Acyltransferase	scaffold_4:1299110-1301172		
J	7	56063	N/A	-0.9406	0.9683	Rac GTPase-activating protein BCR/ABR	scaffold_4:2585070-2587573		
J	7	53076	N/A	-0.9896	0.9846	Hypothetical subunit of the Anaphase-promoting complex	scaffold_4:2621369-2624000		
J	7	123646	N/A	-1.1351	0.9875	-	scaffold_4:696664-698079		
J	7	180222	N/A	-0.6891	0.6557	Guanine nucleotide binding protein MIP1 (Cell cycle control)	scaffold_5:1066022-1070583		
J	7	48485	N/A	-0.7212	0.6735	Hypothetical protein	scaffold_5:1701245-1704004		
J	7	56240	N/A	-0.932	0.8251	-	scaffold_5:1806088-1809840		
J	7	48514	N/A	-1.2057	1.0819	hypothetical protein with DNA-binding domain	scaffold_5:1944320-1947079		
J	7	56252	N/A	-0.7217	0.6648	Proteasome α-subunit	scaffold_5:2016828-2017892		
J	7	209327	N/A	-1.5374	1.4659	Fungal transcriptional regulatory protein, N-terminal	scaffold_5:259988-261303		
J	7	53238	N/A	-1.0663	0.9513	Candidate sterol 3-beta-glucosyltransferease	scaffold_5:960384-966455		
J	7	48778	N/A	-1.2342	1.0947	DHHC-type Zn-finger protein	scaffold_6:1209319-1210803		
J	7	53484	N/A	-0.5049	0.5291	-	scaffold_6:1292434-1293567		
J	7	182985	N/A	-0.5897	0.59	ATPase, E1-E2 type	scaffold_6:517108-520941		
J	7	210131	N/A	-0.62	0.5679	-	scaffold_6:714589-715653		
J	7	53442	N/A	-0.6585	0.5843	Related to GCN20.	scaffold_6:739917-742172		
J	7	185579	N/A	-0.9057	0.8598	-	scaffold_8:1320221-1322109		
J	7	41926	N/A	-0.9098	0.8734	Hypothetical G-protein with WD-40 repeat	scaffold_8:1431055-1433039		
J	7	201372	N/A	-0.8663	0.8422	Sac3/GANP domain protein	scaffold_8:214628-216287		
J	7	41530	N/A	-1.0154	0.9364	Hypothetical glycosylphosphatidylinositol anchor synthesis protein	scaffold_8:251957-255224		
J	7	41548	N/A	-0.922	0.9009	-	scaffold_8:308523-309662		
J	7	201307	N/A	-0.7586	0.6798	-	scaffold_8:43426-44125		
J	7	211484	N/A	-0.616	0.6305	TATA box binding protein (TBP)-associated factor, RNA polymerase II	scaffold_9:465744-467228		
J	8	46473	N/A	-1.5912	1.5279	hypothetical short chain dehydrogenase	scaffold_1:1397654-1398654		
J	8	205776	N/A	-1.2635	1.3247	Predicted membrane protein	scaffold_1:1595292-1596650		
J	8	171996	N/A	-0.6889	0.7073	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_1:1801596-1802612		
J	8	135849	N/A	-1.3205	1.3171	-	scaffold_1:1881054-1881873		
J	8	172198	N/A	-0.9799	1.0206	putative cytochrome P450 monooxygenase	scaffold_1:1999513-2001227		
J	8	206058	N/A	-0.9394	0.9066	Hypothetical cystine transporter	scaffold_1:2440454-2441557		
J	8	36173	N/A	-0.9231	0.9332	DEAD/DEAH box helicase	scaffold_1:2555726-2558901		
J	8	46769	N/A	-0.8768	0.9787	-	scaffold_1:3160160-3164162		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	8	36340	N/A	-0.7146	0.7287	Fungal transcriptional regulatory protein	scaffold_1:3316109-3318335		
J	8	36513	N/A	-0.9731	0.9143	Peptidase S26B, eukaryotic signal peptidase	scaffold_1:3803077-3803773		
J	8	46329	N/A	-1.201	1.0665	-	scaffold_1:575921-577228		
J	8	171532	N/A	-0.7835	0.8915	-	scaffold_1:723104-726820		
J	8	212073	N/A	-0.5987	0.5881	RHO protein GDP dissociation inhibitor	scaffold_10:1099498-1100500	50	
J	8	212076	N/A	-1.0923	1.1287	Serine/threonine-specific protein phosphatase	scaffold_10:1101290-1102283	50	
J	8	42726	N/A	-0.7467	0.7792	-	scaffold_10:504403-508283		
J	8	42779	N/A	-0.4163	0.4132	26S proteasome regulatory complex	scaffold_10:681862-684859		
J	8	56775	N/A	-0.7099	0.6807	(arp3) implicated in control of actin polymerization	scaffold_10:734588-736110		
J	8	212637	N/A	-0.854	0.8637	hypothetical protein containing fungal specific transcription factor and fungal transcriptional regulatory protein domains.	scaffold_11:1069790-1072261		
J	8	203129	N/A	-0.7059	0.6933	hypothetical histidine acid phosphatase	scaffold_11:1347988-1349505		
J	8	189018	N/A	-0.7812	0.8974	Hypothetical protein kinase	scaffold_11:424223-425570		
J	8	189049	N/A	-0.7355	0.6979	WD domain, G-beta repeat	scaffold_11:45148-48147	51	
J	8	126443	N/A	-0.8454	0.904	Calcium-responsive transcription coactivator	scaffold_11:48501-49472	51	
J	8	189589	N/A	-0.7069	0.6678	-	scaffold_12:270314-271141		
J	8	43850	N/A	-0.6999	0.6543	Fungal transcriptional regulatory protein, N-terminal	scaffold_12:855584-857067		
J	8	190724	N/A	-1.4666	1.5297	Major facilitator superfamily	scaffold_13:1152422-1153847		
J	8	44103	N/A	-0.582	0.517	-	scaffold_13:410848-411822		
J	8	123304	N/A	-1.0212	1.0727	Amino acid/polyamine transporter	scaffold_13:855265-856893		
J	8	213266	N/A	-0.8136	0.8788	-	scaffold_13:863229-865080		
J	8	50605	N/A	-0.9506	0.9222	hypothetical tetrahydrofolylpolyglutamate synthase	scaffold_13:933675-934925		
J	8	203913	N/A	-0.9861	1.114	Importin-beta, N-terminal	scaffold_14:282310-285532		
J	8	213557	N/A	-0.8753	0.8443	Short-chain dehydrogenase/reductase	scaffold_14:482141-482988		
J	8	57173	N/A	-0.9311	0.8969	Hypothetical fungal transcription factor	scaffold_14:911578-914632		
J	8	54766	N/A	-0.9887	0.8994	Hypothetical protein	scaffold_15:10059-12175		
J	8	50851	N/A	-1.2768	1.3545	Putative prenyltransferase/squalene oxidase	scaffold_15:257827-258912		
J	8	44753	N/A	-0.7859	0.7129	Esterase/lipase/thioesterase	scaffold_15:315137-316303		
J	8	204317	N/A	-1.5939	1.6462	Vacuolar H+-ATPase V0 sector, subunits	scaffold_16:180408-181220		
J	8	45037	N/A	-0.7003	0.7389	Major facilitator superfamily	scaffold_16:268435-270079		
J	8	133806	N/A	-0.5739	0.5986	-	scaffold_16:503422-505145		
J	8	214048	N/A	-1.1664	1.29	Ribosomal protein S2	scaffold_16:690101-692221		
J	8	192658	N/A	-0.8657	0.9371	SCF ubiquitin ligase, Rbx1 component	scaffold_16:845177-845714		
J	8	192427	N/A	-0.6373	0.5906	-	scaffold_16:860737-862157		
J	8	55022	N/A	-0.7527	0.6391	Hypothetical V-type ATPase subunit	scaffold_17:568701-571441		
J	8	54957	N/A	-0.6139	0.6798	Putative GroEL-like chaperone, ATPase	scaffold_17:70449-72402		
J	8	193822	N/A	-1.0971	1.1094	-	scaffold_18:12060-13454		
J	8	214477	N/A	-0.6099	0.6364	NADH-ubiquinone oxidoreductase	scaffold_18:155364-156113		
J	8	214549	N/A	-0.7436	0.7769	-	scaffold_18:460540-462109		
J	8	45447	N/A	-1.0493	1.0193	Predicted E3 ubiquitin ligase	scaffold_18:9050-10445		
J	8	174497	N/A	-0.9682	1.0216	-	scaffold_2:1073967-1075377		
J	8	137523	N/A	-0.9847	1.0057	Actin-related protein Arp2/3 complex subunit	scaffold_2:1580952-1581610		
J	8	207055	N/A	-0.7821	0.759	Candidate Protein tyrosine phosphatase	scaffold_2:2060002-2061987		
J	8	172988	N/A	-0.8662	0.8961	Hypothetical allantoicase. These proteins allow the use of purines as secondary nitrogen sources in nitrogen-limiting conditions through the reaction: allantoate + H(2)0 = (-)-ureidoglycolate + urea.	scaffold_2:2467850-2468923		
J	8	207105	N/A	-0.5391	0.5527	-	scaffold_2:2549271-2551723		
J	8	47085	N/A	-0.7424	0.7803	Hypothetical H+-transporting two-sector ATPase	scaffold_2:2672366-2673640		
J	8	127729	N/A	-1.354	1.5169	Ankyrin	scaffold_2:2718528-2718866		
J	8	174948	N/A	-0.754	0.7622	hypothetical fumarylacetoacetate hydrolase	scaffold_2:3250697-3251564		
J	8	207359	N/A	-0.5911	0.5862	EF-Hand protein superfamily	scaffold_2:3367437-3368581		
J	8	207411	N/A	-1.4503	1.6451	Peptidase	scaffold_2:3547213-3548214	52	
J	8	52449	N/A	-0.8689	0.8201	Candidate pH-response regulator protein palI	scaffold_2:3552760-3554781	52	
J	8	37546	N/A	-0.8315	0.729	-	scaffold_2:3666500-3668074		
J	8	141681	N/A	-0.7079	0.7796	-	scaffold_2:3870492-3871171		
J	8	173303	N/A	-0.9951	0.9268	-	scaffold_2:3984670-3986916		
J	8	198037	N/A	-0.8678	0.9315	Oligosaccharyltransferase, gamma subunit	scaffold_2:4006581-4007756		
J	8	206602	N/A	-0.7914	0.7204	Triosephosphate isomerase	scaffold_2:760105-760953		
J	8	121662	N/A	-0.8436	0.8459	Predicted transcriptional regulator	scaffold_2:791298-793247	53	
J	8	197123	N/A	-0.5306	0.5386	Rab GDI protein	scaffold_2:795990-797813	53	
J	8	195254	N/A	-0.9464	0.8962	Fungal transcriptional regulatory protein	scaffold_24:43015-44782		
J	8	55720	N/A	-0.9418	0.8878	Nonaspanin	scaffold_3:1163175-1167606		
J	8	55802	N/A	-0.5833	0.6231	Cation efflux protein	scaffold_3:2381752-2383195		
J	8	55813	N/A	-0.673	0.713	hypothetical protein with predicted SH3 domain	scaffold_3:2605764-2608368		
J	8	208428	N/A	-0.9454	0.9801	Metallophosphoesterase	scaffold_3:3395999-3396815		
J	8	55683	N/A	-0.9116	1.0087	Glycoside hydrolase, family 47	scaffold_3:620214-622950		
J	8	207741	N/A	-0.5886	0.6072	hypothetical transcription initiation factor TFIIE, β subunit	scaffold_3:837780-838658		
J	8	207758	N/A	-0.7969	0.782	26S proteasome regulatory complex, subunit PSMD9	scaffold_3:907134-908071		
J	8	55980	N/A	-0.7045	0.6947	-	scaffold_4:1191870-1195982		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	8	129126	N/A	-0.9888	1.0207	Notchless-like WD40 repeat-containing protein	scaffold_4:1944640-1948290		
J	8	53034	N/A	-0.8753	0.8334	-	scaffold_4:2363993-2367628		
J	8	133711	N/A	-0.9351	1.0692	hypothetical protein with histone-fold; GO Desc: DNA binding; GO Id: 3677; Interpro Desc: Histone-fold/TFIID-TAF/NF-Y	scaffold_4:2567224-2568496		
J	8	48146	N/A	-1.1767	1.1674	endonuclease	scaffold_4:2617609-2619503		
J	8	38807	N/A	-0.8493	0.9125	protoporphyrinogen oxidase	scaffold_4:420924-422865		
J	8	178034	N/A	-0.6112	0.6593	-	scaffold_4:541640-542497		
J	8	55956	N/A	-0.7034	0.8181	Hypothetical subunit of the 26S proteasome regulatory complex	scaffold_4:732722-734331		
J	8	181548	N/A	-0.8016	0.7974	Zn-finger, DHHC type	scaffold_5:1370858-1372313		
J	8	39997	N/A	-0.9314	1.0311	hypothetical protein with AB-hydrolase associated lipase region and transmembrane motif	scaffold_5:1494171-1495648		
J	8	53119	N/A	-0.8743	0.9538	Sugar transporter	scaffold_5:16253-18267		
J	8	53141	N/A	-0.8818	0.9534	Hypothetical Na+/H+ antiporter	scaffold_5:165593-167538		
J	8	56228	N/A	-1.0257	1.1023	-	scaffold_5:1657707-1659563		
J	8	56124	N/A	-0.9304	0.9251	Glycoside hydrolase, family 5	scaffold_5:186590-191364		
J	8	56247	N/A	-1.2234	1.2442	Phospholipase D. Active site motif	scaffold_5:1953537-1956364		
J	8	39629	N/A	-0.5414	0.596	-	scaffold_5:209085-211490		
J	8	39574	N/A	-1.1816	1.2284	-	scaffold_5:40770-43241		
J	8	56159	N/A	-0.5028	0.4913	Related to phenylalanine-tRNA ligase of Candida albicans	scaffold_5:609254-610866		
J	8	181153	N/A	-0.8337	0.8277	-	scaffold_5:671586-673280	54	
J	8	209479	N/A	-0.6474	0.6818	-	scaffold_5:673701-676860	54	
J	8	134791	N/A	-0.3411	0.3202	-	scaffold_6:1195368-1196492		
J	8	51629	N/A	-0.7064	0.6939	hapE - CCAAT-binding factor, subunit C	scaffold_6:13443-14571		
J	8	200758	N/A	-1.2629	1.2307	Candidate hexokinase	scaffold_6:1495881-1497842		
J	8	48828	N/A	-1.6272	1.6962	Methyltransferase	scaffold_6:1542897-1543761		
J	8	53444	N/A	-0.4039	0.3245	Hypothetical Isocitrate dehydrogenase	scaffold_6:750646-751935		
J	8	182202	N/A	-1.4988	1.4902	DUF821 domain protein. Putative lipopolysaccharide-modifying enzyme;	scaffold_6:969162-970557		
J	8	48750	N/A	-0.6034	0.6465	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_6:990200-993089		
J	8	120762	N/A	-0.9019	0.9429	Hypothetical 5’-3’ exonuclease	scaffold_7:893037-895324		
J	8	53737	N/A	-0.6554	0.6888	Phox-like	scaffold_8:206528-209003		
J	8	121237	N/A	-0.6033	0.6041	deaminase-reductase	scaffold_8:29186-30736		
J	8	49692	N/A	-0.456	0.4979	-	scaffold_9:1245146-1246425		
J	8	49729	N/A	-0.994	0.9152	Hypothetical hsp40 like	scaffold_9:1405642-1406964		
J	8	211733	N/A	-1.0593	1.1966	Phox-like	scaffold_9:1657011-1660368		
J	8	42104	N/A	-0.4266	0.4603	-	scaffold_9:246556-247621		
J	8	56675	N/A	-0.5294	0.5735	Ubiquitin-conjugating enzyme	scaffold_9:417866-418494		
J	8	186468	N/A	-1.0062	0.9988	Fungal transcriptional regulatory protein	scaffold_9:827313-829164		
J	9	118945	N/A	-0.6596	0.7048	DEAD/DEAH box helicase	scaffold_1:1431282-1435615		
J	9	51839	N/A	-0.4786	0.577	Nucleolar GTPase/ATPase	scaffold_1:1512574-1516310		
J	9	205909	N/A	-1.1488	1.1913	ABC transporter associated with fumonisin-like biosyntehetic gene cluster	scaffold_1:1993993-1998674		
J	9	171156	N/A	-0.5862	0.5737	-	scaffold_1:2130154-2131364		
J	9	51926	N/A	-0.8972	1.0075	-	scaffold_1:2182643-2185943		
J	9	171821	N/A	-1.0375	1.0874	Helicase, C-terminal	scaffold_1:2368425-2371001		
J	9	205486	N/A	-0.7461	0.7499	Metallophosphoesterase	scaffold_1:547864-548685		
J	9	212105	N/A	-0.7151	0.7959	-	scaffold_10:1185015-1186248		
J	9	128267	N/A	-0.7155	0.818	-	scaffold_10:1253401-1253712		
J	9	42619	N/A	-1.6421	1.6217	DSBA oxidoreductase	scaffold_10:167414-168301		
J	9	187673	N/A	-0.6569	0.7466	Caspase	scaffold_10:1743540-1744673		
J	9	43035	N/A	-0.3368	0.3498	-	scaffold_10:1931314-1937709		
J	9	188904	N/A	-0.3056	0.357	-	scaffold_11:309119-309754		
J	9	128642	N/A	-0.7753	0.8189	RNA polymerase	scaffold_11:766591-773337		
J	9	54646	N/A	-0.7727	0.9566	DNA mismatch repair protein	scaffold_13:1011766-1014646		
J	9	54665	N/A	-0.9526	1.134	Splicing coactivator SRm160/300	scaffold_13:1159939-1163231		
J	9	54669	N/A	-0.3345	0.3544	-	scaffold_13:1184556-1185355		
J	9	190779	N/A	-0.5115	0.5253	-	scaffold_13:389133-390259		
J	9	190816	N/A	-0.4725	0.5038	-	scaffold_13:516136-518913		
J	9	134658	N/A	-0.5151	0.5728	Hypothetical 3-methyladenine DNA glycosidase	scaffold_13:909580-910605		
J	9	125995	N/A	-0.7691	0.939	-	scaffold_18:119118-120317		
J	9	214517	N/A	-0.8464	0.8698	Hypothetical COP9 signalosome subunit	scaffold_18:344799-346440		
J	9	214665	N/A	-0.7701	0.9078	Hypothetical protease	scaffold_19:291597-293258		
J	9	45662	N/A	-0.9532	1.1108	-	scaffold_19:89037-90743		
J	9	173896	N/A	-1.0344	1.1187	-	scaffold_2:1899160-1900062		
J	9	206452	N/A	-0.7854	0.8204	klpA Kinesin family protein, motor region, KAR3	scaffold_2:311223-314095		
J	9	45859	N/A	-1.0044	1.0031	Protein kinase	scaffold_20:72175-73134		
J	9	125804	N/A	-0.8321	0.9732	-	scaffold_3:1870427-1871385		
J	9	137097	N/A	-0.6393	0.6434	-	scaffold_3:2089342-2089967		
J	9	37663	N/A	-0.7546	0.7774	Fungal specific transcription factor	scaffold_3:29116-32050		
J	9	129801	N/A	-0.3069	0.3779	-	scaffold_3:2969284-2971915		
J	9	37866	N/A	-0.723	0.8108	Predicted membrane protein	scaffold_3:695585-696763		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	9	199297	N/A	-0.5996	0.6332	Nuclear pore complex, Nup214/CAN component	scaffold_4:1261901-1266476		
J	9	179092	N/A	-0.9021	0.9606	Serine/threonine protein kinase	scaffold_4:1798664-1799953		
J	9	199489	N/A	-0.509	0.5588	FOG: RRM domain	scaffold_4:2408588-2409910	55	
J	9	137851	N/A	-0.3574	0.3736	-	scaffold_4:2414333-2414819	55	
J	9	178804	N/A	-0.8454	0.8505	Putative 2-dehydropantoate 2-reductase activity	scaffold_4:2559582-2560799		
J	9	56078	N/A	-0.5303	0.5456	Deduced protein shares amino acid sequence identity with the Saccharomyces cereivisiae YRG054W gene product; eukaryotic initiation factor (eIF) 2A; associates specifically with both 40S subunits and 80 S ribosomes, and interacts genetically with both eIF5b and eIF4E; homologous to mammalian eIF2A.	scaffold_4:2714536-2716890		
J	9	39521	N/A	-0.6836	0.7543	Guanine nucleotide exchange factor	scaffold_4:2822571-2826985		
J	9	134293	N/A	-1.2512	1.315	-	scaffold_4:660878-662207		
J	9	47895	N/A	-0.8177	0.8327	(nimX) p34cdc2 protein kinase. Required for G1 and G2 in A. nidulans	scaffold_4:826598-827787		
J	9	38926	N/A	-0.8444	0.957	Transcription coactivator	scaffold_4:867885-869343		
J	9	181867	N/A	-0.7419	0.8656	Cell division control protein/predicted DNA repair exonuclease	scaffold_6:1033879-1035916		
J	9	53473	N/A	-0.7383	0.8183	-	scaffold_6:1154863-1155521		
J	9	53496	N/A	-0.8238	0.8608	Fungal transcriptional regulatory protein	scaffold_6:1476015-1478925		
J	9	210383	N/A	-1.0863	1.0904	Hypothetical DNA polymerase delta	scaffold_6:1812970-1816391		
J	9	48617	N/A	-0.6242	0.7424	Serine/threonine protein kinase	scaffold_6:207089-210111		
J	9	127824	N/A	-0.7206	0.8138	Sybindin-like protein	scaffold_6:856383-857005		
J	9	49003	N/A	-0.4729	0.5208	-	scaffold_7:576050-577515		
J	9	185487	N/A	-0.6315	0.6767	Hypothetical transcription factor Tfb2	scaffold_8:127830-129391		
J	9	41966	N/A	-0.7835	0.8693	FATC domain	scaffold_8:1559580-1568740		
J	9	53716	N/A	-0.716	0.8144	Ribulose kinase and related carbohydrate kinases	scaffold_8:45304-47302		
J	9	53784	N/A	-0.6551	0.8074	Ras small GTPase, Rab type	scaffold_8:585138-586073		
J	10	35723	N/A	-0.731	0.8895	hypothetical protein; KOG Class: RNA processing and modification; KOG Id: 1869; KOG description: Splicing coactivator SRm160/300, subunit SRm300	scaffold_1:1160338-1162758		
J	10	51848	N/A	-0.8164	0.9558	Amine oxidase	scaffold_1:1598027-1601458		
J	10	55344	N/A	-0.8309	1.0196	(kexB) proprotein convertase kexB	scaffold_1:1617712-1620298		
J	10	205821	N/A	-0.4144	0.4808	HPr serine phosphorylation site	scaffold_1:1656625-1659744		
J	10	172651	N/A	-0.8309	0.9993	Vacuolar sorting protein 9 (VPS9) domain	scaffold_1:1753306-1755817		
J	10	136883	N/A	-1.132	1.0877	-	scaffold_1:1803985-1804674		
J	10	46707	N/A	-0.5979	0.6771	TPR Domain	scaffold_1:2855672-2859124		
J	10	206215	N/A	-0.8442	0.9407	Predicted MYND Zn-finger protein/hormone receptor interactor	scaffold_1:3020288-3020895		
J	10	139052	N/A	-0.6842	0.6559	hypothetical adaptin gamma subunit	scaffold_1:3217749-3220441		
J	10	171101	N/A	-0.49	0.6329	Actin-binding, cofilin/tropomyosin type	scaffold_1:3280433-3281077		
J	10	136905	N/A	-0.8748	0.9149	Candidate Vps32 homologue	scaffold_10:1251719-1252569		
J	10	188048	N/A	-0.8274	0.939	-	scaffold_10:1897993-1899536		
J	10	187010	N/A	-0.8353	0.8957	Hypothetical H+-transporting two-sector ATPase, α/β subunit, central region	scaffold_10:1972542-1976923		
J	10	49828	N/A	-0.6994	0.8652	RNA-processing protein	scaffold_10:511610-514393		
J	10	56942	N/A	-0.8133	0.9397	Gamma-tubulin complex	scaffold_11:1100815-1103670		
J	10	202968	N/A	-1.1045	1.1457	Hypothetical phosphatidylserine decarboxylase-related	scaffold_11:648083-651708		
J	10	138230	N/A	-0.9081	1.0776	Hypothetical subunit of vacuolar ATPase (EC 3.6.3.6)	scaffold_12:168771-169387		
J	10	213067	N/A	-0.9457	1.052	SMP30-like protein	scaffold_13:338627-339832		
J	10	54585	N/A	-0.7365	1.1045	DSBA oxidoreductase	scaffold_13:581703-582547		
J	10	203695	N/A	-0.9218	0.9286	Hypothetical SNARE protein	scaffold_13:815131-816025		
J	10	213261	N/A	-1.0785	1.3068	Hypothetical aspartic protease	scaffold_13:839618-841060		
J	10	54699	N/A	-1.141	1.2665	Hypothetical amidase	scaffold_14:263532-264826		
J	10	50815	N/A	-0.5949	0.6104	Hypothetical UMP-CMP kinase,phosphotransferase activity, phosphate group as acceptor	scaffold_15:122879-123517		
J	10	192380	N/A	-1.0348	1.1543	-	scaffold_15:239405-243237		
J	10	204770	N/A	-0.7194	0.9019	SAP family cell cycle dependent phosphatase-associated protein	scaffold_17:472310-476324		
J	10	57363	N/A	-0.9902	0.9314	-	scaffold_17:562089-568104		
J	10	136603	N/A	-0.9119	1.0253	Hypothetical transcription initiation factor. A putative YEATS domain is present in the sequence	scaffold_17:87648-88534		
J	10	214503	N/A	-0.8303	0.8093	-	scaffold_18:276103-278142		
J	10	214624	N/A	-0.8779	0.9826	Glycosyl transferase, family 8	scaffold_19:23651-25003		
J	10	52284	N/A	-0.5756	0.6903	Hypothetical protein containing an ATP-dependent DNA ligase I motif	scaffold_2:1725086-1727590		
J	10	206990	N/A	-0.7628	0.905	HMG box-containing protein	scaffold_2:1860454-1860923		
J	10	47046	N/A	-1.0111	1.1314	Hypothetical Ras GTPase	scaffold_2:1963877-1964688		
J	10	175382	N/A	-0.6594	0.7703	Hypothetical 3'-5' exonuclease	scaffold_2:2073345-2075315		
J	10	207173	N/A	-1.0116	1.2206	FYVE finger-containing protein	scaffold_2:2722156-2724505		
J	10	47102	N/A	-0.7189	0.835	Protein phosphatase 2A, regulatory B subunit	scaffold_2:2920444-2922899		
J	10	52388	N/A	-0.7589	0.7615	Hypothetical dynamin, very similar to vpsA of A. nidulans	scaffold_2:2979010-2981520		
J	10	120372	N/A	-1.2491	1.3909	Phosphoinositide-specific phospholipase C (PLC)	scaffold_2:3159617-3161736		
J	10	131319	N/A	-0.7889	0.9244	Major facilitator superfamily	scaffold_2:3832415-3834470		
J	10	36811	N/A	-0.9033	1.0332	-	scaffold_2:863762-866485		
J	10	206654	N/A	-0.9835	1.1339	Fungal transcriptional regulatory protein	scaffold_2:896137-899108		
J	10	47399	N/A	-0.5938	0.6508	Aminoacyl-tRNA synthetase, class I	scaffold_3:1534415-1536396		
J	10	176339	N/A	-0.8542	0.9146	hypothetical protein with predicted histone-fold; KOG Class: Transcription; KOG Id: 3902; KOG description: Histone acetyltransferase PCAF/SAGA, subunit SUPT3H/SPT3	scaffold_3:1729498-1731137		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	10	119023	N/A	-0.8479	1.0492	Nucleolar GTPase/ATPase p130	scaffold_3:2129714-2133406		
J	10	55818	N/A	-0.4328	0.5111	Predicted inosine-uridine preferring nucleoside hydrolase	scaffold_3:2643848-2645448		
J	10	128777	N/A	-1.1707	1.2064	Protein prenyltransferase	scaffold_4:1290351-1296311		
J	10	209075	N/A	-0.8703	0.9656	Hypothetical mannosyltransferase activity	scaffold_4:2544580-2547658		
J	10	178329	N/A	-0.9754	1.0641	hypothetical protein with bromodomain and bromo adjacent region	scaffold_4:2868337-2871372		
J	10	47885	N/A	-0.8494	0.9893	-	scaffold_4:740987-741506		
J	10	199220	N/A	-0.6445	0.7296	HECT	scaffold_4:872691-876830		
J	10	200066	N/A	-0.9291	0.938	Hypothetical protein with FHA domain	scaffold_5:1023729-1026026		
J	10	56195	N/A	-0.7463	0.8842	Carbohydrate kinase, FGGY	scaffold_5:1090763-1093828		
J	10	39611	N/A	-0.6886	0.8638	-	scaffold_5:153338-154593		
J	10	181426	N/A	-1.1267	1.3586	WD40 repeat-containing protein	scaffold_5:631362-632837		
J	10	182977	N/A	-0.7971	0.8906	related to short-chain alcohol dehydrogenases)	scaffold_6:1564998-1568520		
J	10	182157	N/A	-0.2994	0.3485	-	scaffold_6:192434-192999		
J	10	40350	N/A	-0.5202	0.5811	Histone	scaffold_6:205489-206120		
J	10	210065	N/A	-0.6766	0.8076	Transmembrane protein	scaffold_6:480952-482885		
J	10	40419	N/A	-0.9833	1.1703	Dolichyl pyrophosphate phosphatase and related acid phosphatases	scaffold_6:504637-505500		
J	10	210141	N/A	-0.7498	0.9139	Peptidase	scaffold_6:731388-733202		
J	10	53443	N/A	-1.12	1.2476	-	scaffold_6:747941-749332		
J	10	210450	N/A	-0.578	0.6307	AMP-dependent synthetase and ligase	scaffold_7:297603-299962		
J	10	41034	N/A	-0.9667	1.1261	Protein kinase	scaffold_7:441179-443729		
J	10	49077	N/A	-0.7176	1.0549	Hypothetical transcription regulator XNP/ATRX, DEAD-box superfamily	scaffold_7:917964-919146		
J	10	141808	N/A	-0.403	0.5669	-	scaffold_7:927265-928336		
J	10	41887	N/A	-0.7669	0.9667	-	scaffold_8:1309509-1311072		
J	10	185119	N/A	-0.6983	0.7495	Hypothetical protein , contains FHA domain	scaffold_8:827028-827519		
J	10	195373	N/A	-1.136	1.3041	Oxysterol-binding protein	scaffold_84:6961-7809		
J	10	42132	N/A	-0.9906	1.1471	hypothetical lipase	scaffold_9:328556-332018		
J	10	42051	N/A	-0.9013	0.907	-	scaffold_9:71984-72437		
J	11	51891	N/A	-0.69	0.8897	-	scaffold_1:1923203-1925149		
J	11	202514	N/A	-0.8545	1.019	-	scaffold_10:1010915-1015348		
J	11	128501	N/A	-0.5853	0.782	Transcription factor	scaffold_10:1155450-1155962		
J	11	49789	N/A	-0.8575	1.329	related to Peptidylprolyl isomerase	scaffold_10:181184-181898		
J	11	54389	N/A	-0.6597	0.8185	-	scaffold_11:1076442-1077247		
J	11	43379	N/A	-0.8698	0.9575	-	scaffold_11:1084902-1086403		
J	11	56941	N/A	-0.8278	1.0109	-	scaffold_11:1096450-1099365		
J	11	43424	N/A	-1.0684	1.2956	UMUC-like DNA-repair protein	scaffold_11:1214127-1217624		
J	11	43191	N/A	-0.4562	0.6878	Peptidase C48, SUMO/Sentrin/Ubl1	scaffold_11:415031-419301		
J	11	50624	N/A	-0.8028	0.8607	hypothetical CHD5 protein. Coiled coil protein	scaffold_13:1072706-1073497		
J	11	213355	N/A	-0.834	1.1117	hypothetical protein with cupin region; KOG Class: Chromatin structure and dynamics; KOG Id: 2132; KOG description: Uncharacterized conserved protein, contains JmjC domain	scaffold_13:1107510-1108475		
J	11	203569	N/A	-0.5402	0.5904	Uncharacterized protein, induced by hypoxia	scaffold_13:541238-541914		
J	11	54610	N/A	-0.8873	1.1109	Histidine kinase	scaffold_13:735659-738599		
J	11	213957	N/A	-0.8153	0.9151	glaA	scaffold_16:444595-446471		
J	11	57263	N/A	-0.9434	1.2485	eIF-2alpha kinase GCN2 ortholog Translation, ribosomal structure and biogenesis	scaffold_16:520519-525562		
J	11	54926	N/A	-0.9535	1.0626	-	scaffold_16:797277-798500		
J	11	214246	N/A	-1.2732	1.4281	P-type ATPase	scaffold_17:210122-215134		
J	11	139507	N/A	-0.4806	0.5035	Transcription initiation factor TFIID, subunit BDF1 and related bromodomain proteins	scaffold_17:347348-349487		
J	11	51182	N/A	-0.8913	1.0589	Hypothetical ubiquitin-protein ligase	scaffold_17:402537-415010		
J	11	45278	N/A	-0.5523	0.8154	L-kynurenine hydrolase	scaffold_17:98073-99626		
J	11	193872	N/A	-0.7555	0.8875	AAA ATPase	scaffold_18:127945-132967		
J	11	214619	N/A	-0.5664	0.7015	Metallophosphoesterase	scaffold_19:18962-20357		
J	11	52257	N/A	-0.5443	0.7122	Ankyrin repeat	scaffold_2:1544814-1547723		
J	11	207187	N/A	-0.9058	0.8962	hypothetical protein with predicted Appr-1-p domain; KOG Class: Chromatin structure and dynamics; KOG Id: 2633; KOG Description: Hismacro and SEC14 domain-containing proteins	scaffold_2:2743508-2744146		
J	11	37314	N/A	-0.5398	0.5914	-	scaffold_2:2936818-2940181		
J	11	37620	N/A	-1.5178	1.5285	gdhB, NAD dependent glutamate dehydrogenase	scaffold_2:3922956-3926440		
J	11	174887	N/A	-0.5684	0.8019	RNA-processing protein, HAT helix	scaffold_2:3940760-3943768		
J	11	55526	N/A	-0.7932	0.9126	Fungal chitin synthase	scaffold_2:609545-615275		
J	11	57451	N/A	-0.3377	0.5319	Hypothetical ATP (CTP):tRNA-specific tRNA nucleotidyltransferase.	scaffold_20:206216-210046		
J	11	143559	N/A	-0.5128	0.7312	-	scaffold_238:84-867		
J	11	55728	N/A	-0.8732	1.1442	DNA topoisomerase II - ATPase-like, with high homology (topB)	scaffold_3:1284496-1289513		
J	11	52666	N/A	-0.6284	0.7943	-	scaffold_3:2008244-2013861		
J	11	176363	N/A	-1.479	1.7893	-	scaffold_3:3219968-3220355		
J	11	177700	N/A	-0.8575	1.0043	Inner centromere protein (INCENP), C-terminal domain	scaffold_3:3335840-3338827		
J	11	38626	N/A	-1.0075	1.2366	hypothetical DEAH-box helicase; KOG Class: RNA processing and modification; KOG Id: 0922; KOG description: DEAH-box RNA helicase	scaffold_3:3449203-3451336		
J	11	52544	N/A	-0.3511	0.4054	-	scaffold_3:583954-586626		
J	11	52986	N/A	-0.4025	0.4881	Lipoprotein	scaffold_4:1510490-1514657		
J	11	208923	N/A	-0.6562	0.7554	-	scaffold_4:1772615-1774831		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	11	48067	N/A	-0.6287	0.8201	Hydroxyindole-O-methyltransferase and related SAM-dependent methyltransferases	scaffold_4:2076245-2077617		
J	11	181484	N/A	-0.8051	1.133	Fungal specific transcription factor	scaffold_5:1020863-1022987	56	
J	11	53244	N/A	-0.6871	0.8197	-	scaffold_5:1026924-1027531	56	
J	11	209594	N/A	-0.545	0.5489	Myosin class II heavy chain	scaffold_5:1075190-1079939		
J	11	180012	N/A	-1.2269	1.3135	GTPase Rab2, small G protein superfamily	scaffold_5:23467-23991		
J	11	39695	N/A	-0.6132	0.838	-	scaffold_5:454078-457151		
J	11	181068	N/A	-0.8543	0.9378	Ras GTPase-activating protein family - IQGAP	scaffold_5:592745-598262		
J	11	199982	N/A	-0.7845	1.1542	-	scaffold_5:736659-737209		
J	11	39781	N/A	-0.4475	0.5462	-	scaffold_5:771147-773023		
J	11	182079	N/A	-0.7787	0.9888	Hypothetical exocyst complex subunit	scaffold_6:14836-17567		
J	11	48846	N/A	-0.6468	0.8831	-	scaffold_6:1618670-1622389		
J	11	40840	N/A	-1.2822	1.5485	-	scaffold_6:1825544-1826980		
J	11	48715	N/A	-0.7305	0.876	Projectin/twitchin and related proteins	scaffold_6:792943-797968		
J	11	56389	N/A	-0.8367	1.4279	α/β hydrolase fold	scaffold_7:184108-185204		
J	11	48994	N/A	-0.6737	0.7674	Negative regulator of transcription	scaffold_7:529900-537126		
J	11	56447	N/A	-0.4083	0.4857	-	scaffold_7:702281-703708		
J	11	46170	N/A	-0.8619	0.9721	-	scaffold_79:107-979		
J	11	49207	N/A	-0.8134	1.0314	-	scaffold_8:105979-108963		
J	11	211200	N/A	-0.8101	1.0697	Snf7 family protein	scaffold_8:1191493-1192477		
J	11	125232	N/A	-0.4486	0.548	Zn-finger, C-x8-C-x5-C-x3-H type	scaffold_8:1279376-1280658		
J	11	53897	N/A	-0.5263	0.6232	-	scaffold_8:1538316-1542034		
J	11	123910	N/A	-0.5005	0.5947	-	scaffold_8:1625309-1626616		
J	11	211092	N/A	-0.3826	0.4552	Deduced protein shares amino acid sequence identity with the Saccharomyces cerevisiae SLH1 gene product; a putative RNA helicase related to Ski2p, involved in translation inhibition of non-poly(A) mRNAs.	scaffold_8:819816-825791		
J	12	130523	N/A	-0.6622	0.8731	FOG: Zn-finger	scaffold_1:2229191-2231434		
J	12	205452	N/A	-0.3252	0.4113	Hypothetical translation initiation factor 4F	scaffold_1:467137-469122		
J	12	42898	N/A	-0.8432	1.0396	Chromodomain-helicase DNA-binding protein	scaffold_10:1089525-1091798		
J	12	212087	N/A	-0.5778	0.9142	-	scaffold_10:1118131-1119622		
J	12	212197	N/A	-0.6376	0.8153	Protein phosphatase 2C-like	scaffold_10:1777655-1779574		
J	12	122948	N/A	-0.5749	0.7583	-	scaffold_10:1822841-1824411		
J	12	43012	N/A	-0.6163	0.9748	-	scaffold_10:1858685-1859584		
J	12	42720	N/A	-0.3109	0.4145	-	scaffold_10:485655-487054		
J	12	42805	N/A	-0.7739	0.9972	-	scaffold_10:764648-765840		
J	12	188335	N/A	-0.5972	0.8797	-	scaffold_11:1150014-1152059		
J	12	43429	N/A	-0.5247	0.7163	Predicted Isochorismatase hydrolase	scaffold_11:1231801-1234308		
J	12	43165	N/A	-0.3254	0.5983	-	scaffold_11:328933-330357		
J	12	212459	N/A	-0.6064	0.7446	Hypothetical TFIIH basal transcription factor complex, subunit SSL2/RAD25	scaffold_11:369474-371992		
J	12	212473	N/A	-0.8365	1.1079	ATPase-like	scaffold_11:409703-411193		
J	12	189272	N/A	-0.38	0.6098	P-type ATPase	scaffold_11:981791-986306		
J	12	43938	N/A	-0.6443	0.7129	-	scaffold_12:1130328-1131823		
J	12	54460	N/A	-0.4987	0.5633	RNA polymerase II, second largest subunit	scaffold_12:190893-194725		
J	12	189440	N/A	-0.6587	0.7532	-	scaffold_12:302871-304935		
J	12	203210	N/A	-0.5689	0.7051	-	scaffold_12:42258-43888		
J	12	43726	N/A	-0.4705	0.7655	-	scaffold_12:488619-489995		
J	12	54513	N/A	-0.6852	0.8316	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 1973; KOG description: Chromatin remodeling protein, contains PHD Zn-finger	scaffold_13:13109-15230		
J	12	57036	N/A	-0.6257	0.8943	-	scaffold_13:382310-383686		
J	12	54566	N/A	-0.5282	0.5791	Hypothetical tyrosyl-tRNA synthetase. Shows similarity with N. crassa tyrosyl-tRNA synthetase	scaffold_13:432807-434884		
J	12	50560	N/A	-0.6843	0.8972	Predicted ubiquitin regulatory protein	scaffold_13:730453-732036		
J	12	213437	N/A	-1.4251	2.0373	related to GH family 1 β-glucosidase of Trichoderm reesei	scaffold_14:155410-157141		
J	12	44432	N/A	-0.9272	1.4484	Helix loop helix transcription factor EB	scaffold_14:268679-269156		
J	12	191446	N/A	-0.6331	0.9952	-	scaffold_14:286216-287436		
J	12	44376	N/A	-0.6109	1.1126	-	scaffold_14:62031-62912		
J	12	57185	N/A	-0.7384	1.0871	Inositol polyphosphate related phosphatase	scaffold_15:12855-16479		
J	12	50998	N/A	-0.7564	0.9422	-	scaffold_16:381818-385695		
J	12	54887	N/A	-0.4338	0.5798	NADP-dependent flavoprotein reductase	scaffold_16:487968-491670		
J	12	51035	N/A	-1.0325	1.3502	hypothetical Peptidase C19, ubiquitin carboxyl-terminal hydrolase 2	scaffold_16:611999-614506		
J	12	214063	N/A	-0.5286	0.604	-	scaffold_16:730674-732477		
J	12	214206	N/A	-0.4102	0.7897	Nucleoside transporter	scaffold_17:125743-127143		
J	12	45252	N/A	-0.507	0.8372	-	scaffold_17:20905-22884		
J	12	45354	N/A	-0.7686	1.1874	Rab6 GTPase activator	scaffold_17:362563-365338		
J	12	214402	N/A	-0.6961	0.9827	Zn-finger, C2H2 type	scaffold_17:626397-627440		
J	12	214413	N/A	-0.896	1.2318	Vacuolar protein sorting-associated protein	scaffold_17:649758-659420		
J	12	204925	N/A	-0.8363	1.0875	-	scaffold_18:235364-236881		
J	12	214434	N/A	-0.6164	0.9146	Fungal transcriptional regulatory protein	scaffold_18:25263-28302		
J	12	193894	N/A	-0.5341	0.7577	-	scaffold_18:352332-352766		
J	12	45461	N/A	-0.6809	0.8881	putative GH family 3 protein	scaffold_18:60505-63826		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	12	194344	N/A	-0.2975	0.4211	-	scaffold_19:67765-69249		
J	12	214636	N/A	-0.5102	0.6988	Metallophosphoesterase	scaffold_19:74735-76511		
J	12	206697	N/A	-0.4493	0.6667	Exocyst component protein and related proteins	scaffold_2:1048262-1050280		
J	12	36909	N/A	-0.3492	0.6869	hypothetical protein with predicted Protein kinase activity; KOG Class: Chromatin structure and dynamics; KOG Id: 2510; KOG Description: SWI-SNF chromatin-remodeling complex protein	scaffold_2:1212533-1215529		
J	12	206831	N/A	-0.4488	0.6669	Histone acetyltransferase complex	scaffold_2:1466612-1468238		
J	12	52294	N/A	-0.8848	1.0261	Hypothetical protein with AT-rich interaction region	scaffold_2:1799437-1802385		
J	12	206983	N/A	-0.7626	0.9803	-	scaffold_2:1851789-1855637		
J	12	207169	N/A	-0.677	0.7966	Receptor-activated Ca2+-permeable cation channels	scaffold_2:2703790-2705922		
J	12	207175	N/A	-0.6764	0.97	Most probable candidate for a Ca2+-transporting ATPase (EC 3.6.3.8)	scaffold_2:2725054-2731260		
J	12	207326	N/A	-0.5937	0.9583	-	scaffold_2:3312638-3313703		
J	12	52427	N/A	-0.6584	0.8191	Mitochondrial carrier proteins	scaffold_2:3334147-3335576		
J	12	207405	N/A	-0.7413	1.0191	ABC1 family	scaffold_2:3500530-3505716		
J	12	52452	N/A	-0.8566	1.2295	hypothetical α-amylase; EC 3.2.1.1	scaffold_2:3580278-3582162		
J	12	52492	N/A	-0.4594	0.5607	RNA-binding protein	scaffold_2:3948868-3952287		
J	12	206645	N/A	-0.6724	0.8938	related to phosphatidylinositol/phosphatidylglycerol transfer protein	scaffold_2:870567-871214		
J	12	205206	N/A	-0.5616	0.7989	Hypothetical mitochondrial carrier protein	scaffold_20:181729-183111		
J	12	55805	N/A	-0.6432	0.9801	Hypothetical catalytic protein	scaffold_3:2388959-2390468		
J	12	38446	N/A	-0.904	1.4149	-	scaffold_3:2866007-2867758		
J	12	124094	N/A	-0.5767	1.0815	-	scaffold_3:3199043-3200290		
J	12	207638	N/A	-0.7773	1.0261	Golgi-associated protein/Nedd4 WW domain-binding protein	scaffold_3:569149-570407	57	
J	12	119138	N/A	-0.4832	0.6849	-	scaffold_3:574421-578439	57	
J	12	120291	N/A	-0.6492	0.9542	ABC transporter	scaffold_3:761797-764270		
J	12	177655	N/A	-0.7246	0.9929	Cdc4 and related F-box and WD-40 proteins	scaffold_3:799413-802687		
J	12	207773	N/A	-1.0836	1.7399	-	scaffold_3:972246-973285		
J	12	199345	N/A	-0.5364	0.8405	Hypothetical F-actin capping protein, α subunit	scaffold_4:1442469-1443645		
J	12	208882	N/A	-0.661	0.9117	Fungal transcriptional regulatory protein. Has similarity to A. nidulans prnA	scaffold_4:1611537-1614327		
J	12	56013	N/A	-0.4216	0.5507	Serine/threonine kinase	scaffold_4:1722994-1723830		
J	12	179102	N/A	-0.7824	0.9701	-	scaffold_4:235906-236619		
J	12	178271	N/A	-0.4104	0.5131	KOG2013 SMT3/SUMO-activating complex, catalytic component UBA2	scaffold_4:246224-248443		
J	12	53066	N/A	-0.679	0.9689	Guanine nucleotide exchange factor	scaffold_4:2551383-2553596		
J	12	47821	N/A	-0.5644	0.817	Ras small GTPase, Ras type	scaffold_4:370692-371407		
J	12	38797	N/A	-0.4926	0.9556	D-isomer specific 2-hydroxyacid dehydrogenase	scaffold_4:381796-382821		
J	12	52888	N/A	-0.5277	0.7783	-	scaffold_4:522958-524955		
J	12	38681	N/A	-0.5241	0.7312	Peptidase S9	scaffold_4:7644-9714		
J	12	208722	N/A	-0.4464	0.6664	-	scaffold_4:848759-851650		
J	12	38935	N/A	-0.5253	0.7222	Fungal specific transcription factor	scaffold_4:884267-886745		
J	12	181306	N/A	-0.8397	1.205	Basic-leucine zipper (bZIP) transcription factor	scaffold_5:1087383-1088429		
J	12	53262	N/A	-0.6472	0.9833	-	scaffold_5:1214205-1217691		
J	12	180070	N/A	-0.3607	0.572	hypothetical short chain dehydrogenase	scaffold_5:1546716-1547663		
J	12	200271	N/A	-0.5597	0.8663	Zn-finger-like, PHD finger	scaffold_5:1771178-1774760		
J	12	128609	N/A	-0.4416	0.7726	Fructose-6-phosphate 2-kinase/fructose-2,6-biphosphatase	scaffold_5:1988349-1997526		
J	12	209509	N/A	-0.8795	1.1259	WD domain, G-beta repeat	scaffold_5:763930-768297		
J	12	200777	N/A	-0.5936	0.9423	Hypothetical mitotic spindle checkpoint protein	scaffold_6:1554461-1555294		
J	12	200845	N/A	-0.7309	0.9147	Phospholipase D/Transphosphatidylase	scaffold_6:1788576-1792445		
J	12	128466	N/A	-0.3595	0.3936	-	scaffold_6:285020-285319		
J	12	183042	N/A	-0.4126	0.536	-	scaffold_6:416236-417446		
J	12	124595	N/A	-0.604	1.0489	Possible oxidoreductase	scaffold_6:492132-493247		
J	12	210170	N/A	-0.8111	0.9389	-	scaffold_6:861600-865568		
J	12	210716	N/A	-1.0949	1.4525	Glycoside hydrolase, family 5	scaffold_7:1321187-1323651		
J	12	53577	N/A	-0.6433	0.8685	-	scaffold_7:346828-348225		
J	12	210481	N/A	-0.5642	0.9497	Predicted dehydrogenase	scaffold_7:366780-367835		
J	12	56414	N/A	-0.575	0.9792	-	scaffold_7:405649-409399		
J	12	210581	N/A	-0.6524	0.9219	-	scaffold_7:579724-580724		
J	12	183718	N/A	-0.5346	0.9023	Predicted membrane protein	scaffold_7:599822-602910		
J	12	56449	N/A	-0.812	1.0429	-	scaffold_7:716924-720211		
J	12	53632	N/A	-0.8901	1.3367	-	scaffold_7:779538-782610		
J	12	56457	N/A	-0.9063	1.3031	(cmkB) calcium/calmodulin dependent protein kinase B - high homology to cmkB in A. nidulans	scaffold_7:800455-801882		
J	12	53856	N/A	-0.6586	1.0916	Protein phosphatase	scaffold_8:1162245-1164035		
J	12	185306	N/A	-0.7705	1.0801	Short-chain dehydrogenase/reductase	scaffold_8:1302343-1303325		
J	12	185545	N/A	-0.5363	0.8288	-	scaffold_8:1488898-1490744		
J	12	211308	N/A	-0.9617	1.1896	Hypothetical. RNA processing. Related to S. cerev. Lsm4p, involved in mRNA decay; possibly involved in processing tRNA, snoRNA, and rRNA.	scaffold_8:1584285-1587589		
J	12	201495	N/A	-0.7677	1.0438	-	scaffold_8:600128-601135		
J	12	184622	N/A	-0.7093	0.929	-	scaffold_8:73704-75938		
J	12	49737	N/A	-0.6594	0.825	Hypothetical protein	scaffold_9:1437336-1440009		
J	12	56667	N/A	-0.7638	1.0491	Ankyrin repeat protein	scaffold_9:360112-362161		
J	13	51810	N/A	-0.5062	0.8149	Glutathione S-transferase	scaffold_1:1280678-1281601		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	13	206006	N/A	-0.6381	0.7516	Hypothetical protein with calcium-binding EF-hand	scaffold_1:2279639-2283789		
J	13	170766	N/A	-0.669	0.8781	WD domain, G-beta repeat	scaffold_1:2388516-2392160		
J	13	196715	N/A	-0.7765	1.3032	-	scaffold_1:3005702-3008240		
J	13	51738	N/A	-0.6635	0.8527	-	scaffold_1:528542-530225	58	
J	13	195992	N/A	-0.3477	0.6838	Hypothetical cyclic-AMP phosphodiesterase	scaffold_1:532341-534145	58	
J	13	127313	N/A	-0.7028	1.0613	Cysteine dioxygenase CDO1	scaffold_10:1057206-1058192		
J	13	212091	N/A	-0.3535	0.5223	-	scaffold_10:1129723-1131810		
J	13	187334	N/A	-0.5755	0.8393	-	scaffold_10:1140513-1141844		
J	13	42949	N/A	-0.7798	1.0679	-	scaffold_10:1233340-1235753		
J	13	54217	N/A	-0.8069	1.0344	Conserved Zn-finger protein	scaffold_10:1708817-1709472		
J	13	54229	N/A	-0.7	0.9541	-	scaffold_10:1759822-1762079		
J	13	212193	N/A	-0.3633	0.6498	-	scaffold_10:1769144-1770846		
J	13	211845	N/A	-0.6609	0.8198	Glycosyl transferase, family 15	scaffold_10:434651-436389		
J	13	186956	N/A	-0.4154	0.6128	-	scaffold_10:515448-520471		
J	13	211983	N/A	-0.7952	1.0322	Serine/threonine protein kinase	scaffold_10:860952-862646		
J	13	54165	N/A	-0.6781	0.9207	-	scaffold_10:926108-929671		
J	13	56877	N/A	-0.4637	0.8196	Ribosomal protein L35	scaffold_11:168468-173561		
J	13	56896	N/A	-0.524	0.7673	Polyketide synthase	scaffold_11:339265-345944		
J	13	56866	N/A	-0.6304	1.2712	Mitochondrial carrier proteins	scaffold_11:42774-43860		
J	13	54486	N/A	-0.7344	1.2548	-	scaffold_12:518378-520222		
J	13	203222	N/A	-0.5708	0.774	C2 domain protein	scaffold_12:72244-76533		
J	13	50444	N/A	-0.621	0.9889	Serine/threonine protein kinase Atg1	scaffold_13:207130-210179		
J	13	190329	N/A	-0.6286	0.942	Hypothetical SOK1 kinase	scaffold_13:768189-770111		
J	13	57089	N/A	-0.7652	1.1231	DNA-binding SAP	scaffold_13:843725-844630		
J	13	50676	N/A	-0.5557	0.6678	putative Inositol polyphosphate related phosphatase	scaffold_14:198625-201798		
J	13	54733	N/A	-0.6458	0.9704	Eukaryotic transcription factor with helix-loop-helix DNA-binding domain	scaffold_14:515315-518278		
J	13	54806	N/A	-0.657	0.9158	-	scaffold_15:317486-318297		
J	13	119117	N/A	-0.4266	0.684	hypothetical DNA glycosylase	scaffold_15:347450-352093		
J	13	192414	N/A	-1.1711	1.5546	Predicted sugar kinase	scaffold_16:815236-816700		
J	13	214220	N/A	-0.6549	0.7245	-	scaffold_17:145651-147131		
J	13	214360	N/A	-0.7992	1.2028	Xanthine dehydrogenase	scaffold_17:535520-539749		
J	13	141277	N/A	-0.3768	0.6885	-	scaffold_17:559771-561243		
J	13	57394	N/A	-0.6141	1.0702	-	scaffold_18:177517-178847		
J	13	214534	N/A	-0.4922	0.5803	Endoplasmic Reticulum Oxidoreductin 1 (ERO1)	scaffold_18:417305-419051		
J	13	57408	N/A	-0.6203	0.8671	Predicted membrane protein	scaffold_18:464832-465585		
J	13	55089	N/A	-0.4806	0.5176	The basic-leucine zipper (bZIP) transcription factors of eukaryotes are proteins that contain a basic region mediating sequence-specific DNA-binding followed by a leucine zipper region required for dimerization	scaffold_18:507239-509221		
J	13	55091	N/A	-0.8185	0.893	-	scaffold_18:522894-524156		
J	13	214585	N/A	-0.4064	0.6699	Related to Switch Independent protein, Sin3p, and is predicted to contain paired amphiphatic helix (PAH) repeat. Sin3p is scaffold protein part of a co-repressor complex, which silences the transcription by recruiting other proteins deacetylating the histones and leaves chromatin in a repressed state; KOG Class: Chromatin structure and dynamics; KOG Id: 4204; KOG Description: Histone deacetylase complex, catalytic component Sin3p	scaffold_18:544937-550232		
J	13	134668	N/A	-0.9297	1.293	-	scaffold_2:1509444-1510118		
J	13	173811	N/A	-1.5036	2.3299	-	scaffold_2:1520421-1521641		
J	13	197370	N/A	-1.0871	1.3821	-	scaffold_2:1555268-1558787		
J	13	55574	N/A	-0.566	0.7191	Protein kinase	scaffold_2:1709643-1714542		
J	13	37080	N/A	-0.9474	1.1425	pepE, extracellular aspartic protease	scaffold_2:1810758-1812159		
J	13	52118	N/A	-0.6924	1.4703	-	scaffold_2:281001-282294		
J	13	207456	N/A	-0.3758	0.4914	Projectin/twitchin and related proteins	scaffold_2:3742197-3746372		
J	13	197060	N/A	-0.9717	1.2493	Chitin synthase/hyaluronan synthase	scaffold_2:600059-605487		
J	13	52603	N/A	-0.6166	0.8899	related to carboxypeptidase Y	scaffold_3:1234035-1235770		
J	13	125756	N/A	-0.7543	1.2266	-	scaffold_3:1750614-1751756		
J	13	55758	N/A	-0.682	0.9716	Zn-finger, AN1-like	scaffold_3:1910699-1910917		
J	13	47481	N/A	-0.3232	0.3448	Protein phosphatase 2C-like	scaffold_3:1999550-2000692		
J	13	47550	N/A	-0.398	0.5047	-	scaffold_3:2354109-2355132		
J	13	208158	N/A	-0.574	0.8718	Protein kinase	scaffold_3:2602387-2604327		
J	13	55835	N/A	-0.6515	0.8826	related to voltage-gated calcium channel	scaffold_3:2808152-2814621		
J	13	208293	N/A	-0.5049	0.7034	hypothetical Silent Information regulator protein Sir2p (family); KOG Class: Chromatin structure and dynamics; KOG Id: 2684; KOG Description: Sirtuin 5 and related class III sirtuins (SIR2 family)	scaffold_3:3008988-3010923		
J	13	208321	N/A	-0.719	0.834	Peroxisomal membrane protein MPV17 and related proteins	scaffold_3:3095535-3096699		
J	13	55859	N/A	-0.4089	0.4826	DEAD/DEAH box helicase	scaffold_3:3107127-3111735		
J	13	208365	N/A	-0.7134	1.0604	Hypothetical. KOG: aldo/keto reductase	scaffold_3:3209564-3212599		
J	13	55897	N/A	-0.6714	0.9746	Haem peroxidase, plant/fungal/bacterial	scaffold_3:3473541-3475658		
J	13	37772	N/A	-0.6663	0.7815	hypothetical fungal specific transcription factor and N-6 Adenine-specific DNA methylase	scaffold_3:386823-389345		
J	13	120278	N/A	-0.7534	1.2815	Serine/threonine dehydratase	scaffold_3:814357-816615		
J	13	39109	N/A	-0.611	0.7848	-	scaffold_4:1440060-1442050		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	13	208930	N/A	-0.6745	1.1822	Silent information regulator protein Sir2	scaffold_4:1779827-1780837		
J	13	178187	N/A	-0.5965	0.8489	Hypothetical palmitoyltransferase	scaffold_4:2540569-2542527		
J	13	53096	N/A	-0.4199	0.5474	Myosin class II heavy chain	scaffold_4:2816581-2821628		
J	13	39552	N/A	-0.8314	1.2177	-	scaffold_4:2917977-2918926		
J	13	178015	N/A	-0.6591	0.8785	Protein phosphatase	scaffold_4:402384-409430		
J	13	178051	N/A	-0.7898	1.3095	Related to A. nidulans CreC	scaffold_4:774967-776995		
J	13	39960	N/A	-0.5276	0.9886	-	scaffold_5:1337838-1338781		
J	13	53140	N/A	-0.5959	0.7966	FMN-dependent dehydrogenase	scaffold_5:149495-151136		
J	13	200208	N/A	-0.6087	0.7101	N-methyl-D-aspartate receptor glutamate-binding subunit	scaffold_5:1609210-1610173		
J	13	180108	N/A	-0.6466	1.1275	-	scaffold_5:1665338-1666642	59	
J	13	48479	N/A	-0.5687	0.7661	-	scaffold_5:1669005-1670687	59	
J	13	48505	N/A	-0.5837	0.8616	-	scaffold_5:1826079-1827261		
J	13	56133	N/A	-0.9465	1.1357	ABC superfamily	scaffold_5:312946-316349		
J	13	56179	N/A	-0.6247	0.7527	Tyrosine specific protein phosphatase and dual specificity protein phosphatase	scaffold_5:866222-868357		
J	13	40734	N/A	-0.3592	0.6344	Hypothetical aldehyde dehydrogenase. Specificity towards NAD or NADP is not deducible from sequence data	scaffold_6:1487104-1488577		
J	13	181938	N/A	-0.4514	0.7284	Ypt/Rab-specific GTPase-activating protein GYP7 and related proteins	scaffold_6:537960-540695		
J	13	123110	N/A	-0.5368	0.7907	Predicted gamma-butyrobetaine,2-oxoglutarate dioxygenase	scaffold_6:900260-901393		
J	13	184220	N/A	-0.3994	0.5178	-	scaffold_7:242617-243842		
J	13	48938	N/A	-0.7587	0.9925	WD40-like repeat containing protein	scaffold_7:314992-317552		
J	13	56422	N/A	-0.6057	0.9533	-	scaffold_7:455159-457588		
J	13	53643	N/A	-0.496	0.6041	-	scaffold_7:822235-823951		
J	13	211143	N/A	-0.4259	0.6903	Pyridoxamine-phosphate oxidase	scaffold_8:1020251-1021410		
J	13	56523	N/A	-0.8496	1.3966	related to leucine aminopeptidase	scaffold_8:185032-186340		
J	13	201415	N/A	-0.775	0.9958	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_8:305578-306556		
J	13	42404	N/A	-1.0033	1.4931	-	scaffold_9:1131238-1133082		
J	13	211680	N/A	-0.6764	0.7302	-	scaffold_9:1442584-1445358		
J	13	186864	N/A	-0.5083	0.7522	-	scaffold_9:1648872-1652469		
J	13	53931	N/A	-0.5607	0.9348	Putative Cyclin possibly similar to Pcl5	scaffold_9:177054-179249	60	
J	13	124867	N/A	-0.37	0.5424	putative extracellular protein	scaffold_9:180574-181272	60	
J	14	35916	N/A	-1.1925	1.1253	Caspase-1, p20	scaffold_1:1751453-1752998		
J	14	51896	N/A	-0.6609	0.6132	Hypothetical. KOG suggests role in cell division	scaffold_1:1961078-1963396		
J	14	170638	N/A	-0.7049	0.7802	-	scaffold_1:2097579-2098229		
J	14	212098	N/A	-0.7666	0.6532	Hypothetical CAP20-like protein	scaffold_10:1171489-1172122		
J	14	119175	N/A	-1.2482	1.0446	Ank repeat	scaffold_10:125159-129200		
J	14	211766	N/A	-0.7246	0.8172	SAM (and some other nucleotide) binding motif	scaffold_10:144939-145688		
J	14	186948	N/A	-0.6377	0.5334	-	scaffold_10:1853831-1855807	61	
J	14	122702	N/A	-0.8813	0.6856	-	scaffold_10:1860035-1862375	61	
J	14	54294	N/A	-0.6228	0.6957	-	scaffold_11:165955-166973		
J	14	189289	N/A	-0.5203	0.507	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 2510; KOG Description: SWI-SNF chromatin-remodeling complex protein	scaffold_11:758792-762975		
J	14	54462	N/A	-0.7436	0.5803	hypothetical PHD finger and Zn finger-like protein	scaffold_12:205018-206274		
J	14	190167	N/A	-0.8401	0.8526	Homeobox protein	scaffold_12:78268-80025		
J	14	44301	N/A	-0.6445	0.5436	-	scaffold_13:1016160-1017550		
J	14	50512	N/A	-0.4637	0.4831	hypothetical SWI-SNF chromatin-remodeling complex protein	scaffold_13:548919-551629		
J	14	190278	N/A	-0.7376	0.7325	-	scaffold_13:760802-761659		
J	14	190790	N/A	-0.3816	0.3432	related to sporulation specific gene SPS2	scaffold_13:902677-903895		
J	14	203868	N/A	-0.4858	0.5007	Aromatic-ring hydroxylase	scaffold_14:132836-134182		
J	14	191326	N/A	-0.7426	0.8005	-	scaffold_14:316452-318826		
J	14	191251	N/A	-0.7598	0.8053	D-arabinose-1,4-lactone oxidase	scaffold_14:75003-76745		
J	14	57200	N/A	-0.9264	0.7524	-	scaffold_15:187223-188625		
J	14	54797	N/A	-0.4331	0.3253	Predicted proline-serine-threonine phosphatase-interacting protein	scaffold_15:210758-213638		
J	14	192051	N/A	-0.7664	0.7962	Putative GTPase activating proteins	scaffold_15:60842-64577		
J	14	129924	N/A	-1.0092	1.0365	-	scaffold_15:689102-691459		
J	14	54964	N/A	-1.1343	1.1036	-	scaffold_17:107370-108619		
J	14	214265	N/A	-1.0141	0.9831	putative polyubiquitin	scaffold_17:268153-269213		
J	14	55013	N/A	-0.5304	0.5119	Hypothetical protein.	scaffold_17:501276-505216		
J	14	54961	N/A	-0.8354	0.5945	hypothetical cysteine dioxygenase (EC 1.13.11.20)	scaffold_17:92023-92787		
J	14	132225	N/A	-0.6805	0.7391	-	scaffold_18:340378-342104		
J	14	197446	N/A	-0.9019	0.9762	candidate GH family 18 endo-chitinase	scaffold_2:1767698-1769324		
J	14	47062	N/A	-0.7297	0.7874	-	scaffold_2:2441179-2441761		
J	14	37188	N/A	-0.7492	0.6288	Sensory transduction histidine kinase	scaffold_2:2459900-2467200		
J	14	207158	N/A	-1.2392	0.9577	Prohibitins and stomatins of the PID superfamily	scaffold_2:2687391-2688608	62	
J	14	207161	N/A	-0.4586	0.3844	-	scaffold_2:2692370-2695427	62	
J	14	37333	N/A	-1.16	1.1317	-	scaffold_2:3010249-3012851		
J	14	37344	N/A	-0.8655	0.9704	Inositol polyphosphate 5-phosphatase and related proteins	scaffold_2:3051399-3055362		
J	14	174236	N/A	-1.1679	1.0314	-	scaffold_2:3336393-3337112	63	
J	14	173936	N/A	-1.0148	1.0054	-	scaffold_2:3337784-3339078	63	

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	14	119798	N/A	-0.5417	0.5623	Splicing coactivator SRm160/300	scaffold_2:3516569-3519016		
J	14	207424	N/A	-0.9517	0.7708	Hypothetical major intrinsic protein	scaffold_2:3583597-3584502		
J	14	52480	N/A	-0.7614	0.7808	-	scaffold_2:3853484-3855927		
J	14	197098	N/A	-0.4857	0.4255	Golgi proteins involved in ER retention	scaffold_2:734633-735425		
J	14	206607	N/A	-1.6683	1.6076	hypothetical ribose-5-phosphate isomerase	scaffold_2:763800-764288		
J	14	174635	N/A	-0.447	0.4334	Peptidase	scaffold_2:826745-829492		
J	14	46133	N/A	-0.7509	0.8556	-	scaffold_24:114893-116641		
J	14	55770	N/A	-0.7203	0.7377	hypothetical protein containing Zn-finger,C2H2 type domain	scaffold_3:2027115-2028013		
J	14	177723	N/A	-0.5698	0.6434	-	scaffold_3:2868690-2870121		
J	14	55909	N/A	-0.5641	0.5086	GTP binding protein	scaffold_3:3550830-3552184		
J	14	37789	N/A	-0.8003	0.7067	Shares amino acid sequence identity with Saccharomyces cerevisiae GCD1 gene product comprising the gamma subunit of the translation initiation factor eIF2B; the guanine-nucleotide exchange factor for eIF2; activity subsequently regulated by phosphorylated eIF2.	scaffold_3:439664-441344		
J	14	52539	N/A	-1.0083	1.0266	-	scaffold_3:532147-533076		
J	14	47281	N/A	-0.3287	0.3675	Coeffector of mDia Rho GTPase, regulates actin polymerization and cell adhesion turnover	scaffold_3:623796-626257		
J	14	207660	N/A	-0.7577	0.702	Glycosyl transferase, family 48	scaffold_3:632144-637969		
J	14	208780	N/A	-0.3749	0.4106	Protein kinase	scaffold_4:1179893-1182571		
J	14	52970	N/A	-1.0957	1.1878	-	scaffold_4:1353492-1357448		
J	14	208913	N/A	-0.9414	0.7586	Predicted Cytosolic sorting protein GGA2/TOM1	scaffold_4:1751467-1752853		
J	14	208985	N/A	-1.446	1.2671	EF hand	scaffold_4:2380488-2382751		
J	14	124830	N/A	-0.4344	0.3337	Short-chain dehydrogenase/reductase	scaffold_4:244756-245816		
J	14	38832	N/A	-0.6808	0.7914	Cytochrome P450	scaffold_4:515977-517804		
J	14	133628	N/A	-0.516	0.5568	-	scaffold_5:1146807-1148132		
J	14	180300	N/A	-0.3172	0.3986	Uncharacterized conserved protein, contains WD40 repeats	scaffold_5:1260326-1261726		
J	14	129504	N/A	-1.0511	1.0449	AAA+-type ATPase	scaffold_5:1981806-1983637		
J	14	123918	N/A	-0.5137	0.4573	Translocase of outer mitochondrial membrane complex	scaffold_5:538103-539460		
J	14	40728	N/A	-0.4612	0.3903	-	scaffold_6:1469868-1470959		
J	14	56378	N/A	-0.4574	0.4954	-	scaffold_6:1778851-1780906		
J	14	53546	N/A	-1.0063	0.9038	Putative Aconitate hydratase	scaffold_6:1939200-1942032		
J	14	48718	N/A	-0.9008	0.8493	-	scaffold_6:820679-821359		
J	14	40575	N/A	-0.62	0.709	-	scaffold_6:999512-1001295		
J	14	210711	N/A	-0.6605	0.6412	Hypothetical protein. May be part of the WD40 superfamily	scaffold_7:1310052-1312683		
J	14	41045	N/A	-0.4759	0.3287	Esterase/lipase/thioesterase	scaffold_7:469289-470328		
J	14	184678	N/A	-0.5167	0.5654	-	scaffold_8:1031117-1031647		
J	14	53758	N/A	-0.8989	0.7455	-	scaffold_8:382433-384328		
J	14	53770	N/A	-1.5793	1.3198	hypothetical GPI anchor protein	scaffold_8:469884-470480		
J	14	184561	N/A	-0.787	0.8247	Rhodopsin-like GPCR superfamily	scaffold_8:47733-51071		
J	14	184967	N/A	-0.3147	0.2684	-	scaffold_8:997412-998260		
J	14	211616	N/A	-0.7912	0.8684	Peptidase	scaffold_9:1231343-1233280		
J	14	202087	N/A	-0.5822	0.6205	-	scaffold_9:1263648-1265546		
J	14	42477	N/A	-0.6454	0.6559	Peptidase	scaffold_9:1347941-1355973		
J	15	172690	N/A	-0.7377	0.7281	Hypothetical protein with Cytochrome c heme-binding site	scaffold_1:1840990-1843242		
J	15	205944	N/A	-0.5123	0.4893	-	scaffold_1:2108356-2109206		
J	15	206311	N/A	-0.8707	0.8762	-	scaffold_1:3286340-3287516		
J	15	187777	N/A	-0.4874	0.5488	3-oxo-5-alpha-steroid 4-dehydrogenase, C-terminal	scaffold_10:1021641-1022763		
J	15	212262	N/A	-0.5973	0.7471	-	scaffold_10:1939838-1941410		
J	15	42657	N/A	-0.6507	0.6307	-	scaffold_10:282723-284019		
J	15	54114	N/A	-0.5248	0.6376	RhoGEF domain	scaffold_10:522911-527681		
J	15	211968	N/A	-0.3156	0.334	Fungal specific transcription factor	scaffold_10:800752-803826		
J	15	188462	N/A	-0.4364	0.5663	Acyltransferase	scaffold_11:1173961-1175589		
J	15	56955	N/A	-0.6122	0.7391	Ketopantoate reductase ApbA/PanE	scaffold_11:1461573-1462562		
J	15	212570	N/A	-0.8289	0.8699	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 1020; KOG Description: Sister chromatid cohesion protein SCC2/Nipped-B	scaffold_11:780177-781343		
J	15	212597	N/A	-0.4032	0.3964	Cytochrome P450	scaffold_11:899894-910072		
J	15	54373	N/A	-0.6085	1.0247	-	scaffold_11:924163-926163		
J	15	203304	N/A	-0.8004	0.7183	-	scaffold_12:313203-316567		
J	15	54525	N/A	-0.4825	0.6446	Ornithine aminotransferase otaA (EC 2.6.1.13)	scaffold_13:161928-163363	64	
J	15	190230	N/A	-0.5541	0.5254	-	scaffold_13:164336-168868	64	
J	15	213031	N/A	-0.4857	0.5089	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_13:195710-197684	65	
J	15	128887	N/A	-0.5381	0.49	Phosphatidate cytidylyltransferase	scaffold_13:199001-204553	65	
J	15	190335	N/A	-0.6924	0.839	Protein kinase	scaffold_13:256874-259026		
J	15	44405	N/A	-0.4276	0.6358	Hypothetical DNA excision repair protein	scaffold_14:151216-152415		
J	15	213457	N/A	-0.7122	0.6716	-	scaffold_14:260771-261520		
J	15	44921	N/A	-0.3768	0.4319	-	scaffold_15:852978-853584		
J	15	57265	N/A	-1.1258	1.8519	gatA, 4-aminobutyrate aminotransferase	scaffold_16:534578-536270		
J	15	193476	N/A	-0.7003	0.6143	Hypothetical Mitochondrial matrix protein frataxin,	scaffold_17:343157-343891		
J	15	214353	N/A	-0.7251	0.6143	Nucleolar GTPase/ATPase p130	scaffold_17:510411-511595		
J	15	204833	N/A	-0.6538	0.8544	Hypothetical GDP-mannose pyrophosphorylase/mannose-1-phosphate guanylyltransferase	scaffold_17:640134-641501		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	15	214476	N/A	-0.8086	0.8547	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_18:142331-145966		
J	15	52224	N/A	-1.0738	1.0801	Annexin	scaffold_2:1311592-1312974		
J	15	206906	N/A	-0.9234	1.1979	hypothetical protein with predicted BROMO domain and histone fold, probably involved in transcription; KOG Class: Chromatin structure and dynamics; KOG Id: 1472; KOG Description: Histone acetyltransferase SAGA/ADA, catalytic subunit PCAF/GCN5 and related proteins	scaffold_2:1654266-1657960		
J	15	173250	N/A	-0.3015	0.3823	-	scaffold_2:2615465-2617060	66	
J	15	207131	N/A	-0.9224	1.1314	Nucleolar GTPase/ATPase p130	scaffold_2:2617989-2620162	66	
J	15	197631	N/A	-0.5665	0.6503	-	scaffold_2:2626735-2627717		
J	15	52393	N/A	-0.4436	0.4081	Nucleolar GTPase/ATPase p130	scaffold_2:3033260-3034999		
J	15	36700	N/A	-0.5194	0.444	AAA ATPase	scaffold_2:441155-444049		
J	15	52703	N/A	-0.7617	0.8883	Hypothetical S28 peptidase. Signalp prediction indicates secretion	scaffold_3:2362414-2364523		
J	15	38485	N/A	-0.518	0.573	Homeobox transcription factor	scaffold_3:2991309-2993484		
J	15	177500	N/A	-0.5454	0.677	Esterase/lipase/thioesterase	scaffold_3:3486365-3488711		
J	15	127559	N/A	-1.0648	1.2623	Serine O-acetyltransferase	scaffold_3:3957888-3958373		
J	15	52574	N/A	-0.377	0.41	-	scaffold_3:830992-837124		
J	15	118893	N/A	-0.5777	0.7213	-	scaffold_4:1227478-1231703		
J	15	143109	N/A	-0.3106	0.3172	FOG: Ankyrin repeat	scaffold_4:1494825-1495814		
J	15	209086	N/A	-0.6102	0.556	(racA) Ras-related small GTPase, Rho type	scaffold_4:2578350-2579311		
J	15	209129	N/A	-1.0229	0.8594	-	scaffold_4:2700132-2701481		
J	15	38819	N/A	-0.4957	0.5272	-	scaffold_4:472227-472896		
J	15	38703	N/A	-0.4866	0.5046	hypothetical carboxylesterase	scaffold_4:91563-92888		
J	15	129373	N/A	-0.5788	0.6034	-	scaffold_5:1317383-1324138		
J	15	48502	N/A	-0.7174	0.8032	Hypothetical septin B-like protein	scaffold_5:1818593-1819933		
J	15	181032	N/A	-0.5853	0.7378	Fungal specific transcription factor	scaffold_5:2094449-2096741		
J	15	180396	N/A	-0.5352	0.5958	-	scaffold_5:299601-300751		
J	15	56152	N/A	-0.3282	0.5221	related to Asp f4 allergen of Aspergillus fumigatus	scaffold_5:544209-545198		
J	15	56163	N/A	-0.5695	0.5049	-	scaffold_5:656955-660034		
J	15	53524	N/A	-0.7019	0.7809	-	scaffold_6:1694298-1694792		
J	15	210119	N/A	-2.0253	2.0635	Major facilitator superfamily	scaffold_6:689542-691223		
J	15	56329	N/A	-0.5271	0.7111	Tubulin/FtsZ, C-terminal	scaffold_6:895806-897636		
J	15	56423	N/A	-0.5417	0.6701	-	scaffold_7:464410-466542		
J	15	53600	N/A	-1.0253	0.8905	Aminotransferase, class-II	scaffold_7:476533-477537		
J	15	211217	N/A	-0.6277	0.7235	-	scaffold_8:1207548-1208729		
J	15	185138	N/A	-0.3009	0.3792	Candidate GCN5-related histone actyltransferase (GNAT)	scaffold_8:1379916-1381202		
J	15	41522	N/A	-0.6217	0.6681	-	scaffold_8:230074-233058		
J	15	201497	N/A	-0.7514	0.4678	-	scaffold_8:605018-605860	67	
J	15	53788	N/A	-0.8615	0.8399	Nucleoside phosphatase	scaffold_8:608459-610790	67	
J	15	41474	N/A	-0.6048	0.6767	-	scaffold_8:76869-77347		
J	15	49354	N/A	-0.4715	0.4711	Glucose/ribitol dehydrogenase	scaffold_8:976929-978420		
J	15	211625	N/A	-0.894	0.9848	Protein kinase	scaffold_9:1278977-1282868		
J	15	56659	N/A	-0.3183	0.3345	-	scaffold_9:260932-261878		
J	15	42138	N/A	-0.4998	0.6189	-	scaffold_9:368707-369380		
J	16	51834	N/A	-1.2582	1.0307	Hypothetical protein	scaffold_1:1470196-1475253		
J	16	196278	N/A	-0.5282	0.4004	Glutamine synthetase	scaffold_1:1534933-1536546		
J	16	51873	N/A	-0.7315	0.6906	cpcA, Cross-pathway control protein A	scaffold_1:1759343-1760137		
J	16	35952	N/A	-0.457	0.4581	-	scaffold_1:1872282-1873402		
J	16	51913	N/A	-0.8805	0.7322	Putative IreA	scaffold_1:2070247-2073737		
J	16	170508	N/A	-0.8967	0.8247	Hypothetical. Nuclease domain	scaffold_1:2508020-2508934		
J	16	55505	N/A	-0.7763	0.4553	Major facilitator superfamily	scaffold_1:3892528-3894194		
J	16	51721	N/A	-0.8153	0.7529	-	scaffold_1:405725-406726		
J	16	54150	N/A	-1.3746	0.9492	-	scaffold_10:788291-789328		
J	16	43484	N/A	-0.594	0.4049	-	scaffold_11:1393644-1394936		
J	16	128442	N/A	-0.6545	0.5303	-	scaffold_11:147012-147281		
J	16	121829	N/A	-0.6104	0.6248	-	scaffold_11:632444-633772		
J	16	127170	N/A	-0.8517	0.6363	-	scaffold_12:177625-178251		
J	16	43607	N/A	-0.9518	0.7927	-	scaffold_12:92050-93178		
J	16	203770	N/A	-0.4685	0.4583	Protein kinase	scaffold_13:1032634-1036188		
J	16	190765	N/A	-1.0062	0.8667	Fungal transcriptional regulatory protein	scaffold_13:171566-173376		
J	16	57027	N/A	-0.6703	0.5879	(phyA) Multiple inositol polyphosphate phosphatase phyA	scaffold_13:325549-327287		
J	16	57072	N/A	-0.5117	0.3693	putative Translation initiation factor 2, gamma subunit (eIF-2gamma; GTPase) Translation, ribosomal structure and biogenesis	scaffold_13:687765-689450		
J	16	44296	N/A	-1.1808	1.0947	-	scaffold_13:976231-976893		
J	16	191425	N/A	-0.9529	0.6252	-	scaffold_14:186112-187531		
J	16	203893	N/A	-0.4905	0.4044	Single-strand binding protein/Primosomal replication protein	scaffold_14:207618-208321		
J	16	121911	N/A	-0.4571	0.4055	Hypothetical UDP-glucose/GDP-mannose dehydrogenase	scaffold_14:82616-84357		
J	16	204050	N/A	-2.6201	2.4198	FAD binding domain	scaffold_14:867281-873572		
J	16	44384	N/A	-0.5278	0.4778	-	scaffold_14:87941-89197		
J	16	44868	N/A	-0.9709	0.8499	-	scaffold_15:671213-673454		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	16	57283	N/A	-0.659	0.5843	This protein is involved in sexual reproduction;	scaffold_16:693819-696279		
J	16	54982	N/A	-0.5575	0.5102	Hypothetical protein with homeobox domain	scaffold_17:231080-232695		
J	16	120847	N/A	-0.8333	0.7304	Hypothetical peptidase with G-protein β WD-40 repeat	scaffold_17:36982-39010		
J	16	204742	N/A	-0.2871	0.2859	Hypothetical protein involved in chromatin remodeling	scaffold_17:388753-390329		
J	16	51181	N/A	-1.8963	1.6016	Cytochrome P450	scaffold_17:397490-401114		
J	16	193171	N/A	-0.927	0.7937	AAA ATPase	scaffold_17:521055-522650		
J	16	55026	N/A	-1.0558	0.8712	Di-trans-poly-cis-decaprenylcistransferase	scaffold_17:587688-588963		
J	16	51304	N/A	-0.9429	0.8328	Might be involved in signal transduction	scaffold_18:433701-435038	68	
J	16	131844	N/A	-0.6187	0.6014	Hypothetical protein with a Myb, DNA-binding domain	scaffold_18:436086-437726	68	
J	16	45614	N/A	-0.4536	0.3536	Predicted protein shares amino acid sequence identity to the Saccharomyces cerevisiae TIF4631 gene product; translation initiation factor eIF4G, subunit of the mRNA cap-binding protein complex (eIF4F) that also contains eIF4E (Cdc33p); associates with the poly(A)-binding protein Pab1p, also interacts with eIF4A (Tif1p); homologous to Tif4632p.	scaffold_18:594137-599172		
J	16	55147	N/A	-0.7456	0.4165	-	scaffold_19:498021-499927		
J	16	206795	N/A	-0.3929	0.2976	NADH-ubiquinone oxidoreductase, chain 49kDa	scaffold_2:1384726-1386282		
J	16	120110	N/A	-0.8307	0.5984	Zn-finger, C2H2 type	scaffold_2:1762932-1765164		
J	16	207006	N/A	-0.9445	0.6815	-	scaffold_2:1889471-1890733		
J	16	37144	N/A	-0.5668	0.4095	-	scaffold_2:2030209-2031192		
J	16	37268	N/A	-0.6739	0.5474	GATA-4/5/6 transcription factors	scaffold_2:2752861-2754716		
J	16	47152	N/A	-1.1011	0.8126	-	scaffold_2:3412907-3413545		
J	16	173430	N/A	-0.6421	0.5671	Major facilitator superfamily	scaffold_2:3681830-3684171		
J	16	55653	N/A	-0.5261	0.5039	-	scaffold_2:3895779-3897620		
J	16	55656	N/A	-0.7711	0.6762	-	scaffold_2:3953369-3955611		
J	16	52158	N/A	-0.8611	0.7724	-	scaffold_2:686115-687264		
J	16	175486	N/A	-0.5305	0.4442	-	scaffold_2:947195-949115		
J	16	52189	N/A	-0.691	0.6248	Protein kinase	scaffold_2:960988-963726		
J	16	175169	N/A	-0.8659	0.7528	-	scaffold_2:999054-999695		
J	16	47372	N/A	-0.5563	0.5036	Peroxidase	scaffold_3:1241736-1242737		
J	16	52657	N/A	-0.8947	0.6798	Actin/actin-like	scaffold_3:1926796-1928413		
J	16	208141	N/A	-0.5056	0.3813	-	scaffold_3:2571329-2572513		
J	16	176581	N/A	-0.7241	0.5456	Predicted haloacid-halidohydrolase and related hydrolases	scaffold_3:3003487-3004460		
J	16	38635	N/A	-0.4869	0.5362	-	scaffold_3:3466343-3468333		
J	16	132526	N/A	-0.5774	0.5359	-	scaffold_3:3496483-3498347		
J	16	207689	N/A	-0.3416	0.332	Peptidase M20	scaffold_3:709993-711547		
J	16	175768	N/A	-0.6768	0.5827	HORMA domain	scaffold_3:805323-808129		
J	16	125186	N/A	-1.0773	0.8268	Dehydrogenase	scaffold_4:1244537-1245789		
J	16	55999	N/A	-0.7508	0.6917	-	scaffold_4:1384619-1386554		
J	16	53008	N/A	-0.9675	0.7431	Hypothetical aminopeptidase	scaffold_4:1775716-1777814		
J	16	38769	N/A	-0.4506	0.3494	-	scaffold_4:297752-299761		
J	16	208591	N/A	-0.7041	0.5983	serine carboxypeptidase	scaffold_4:399057-401383		
J	16	209597	N/A	-0.587	0.3965	Protein kinase	scaffold_5:1082227-1083463		
J	16	48523	N/A	-0.8617	0.5378	-	scaffold_5:2015380-2016409		
J	16	181397	N/A	-1.35	1.157	Hypothetical fatty-acyl coenzyme A oxidase (EC 1.3.3.6).	scaffold_5:2262620-2264873		
J	16	180131	N/A	-0.8248	0.7245	Abl interactor ABI-1, contains SH3 domain	scaffold_5:585947-587020		
J	16	53386	N/A	-0.5841	0.5492	Chitinase	scaffold_6:142926-145142		
J	16	40335	N/A	-0.8314	0.705	Leptin receptor gene-related protein	scaffold_6:166451-167071		
J	16	53522	N/A	-0.4007	0.3868	Hypothetical microtubule-associated protein essential for anaphase spindle elongation	scaffold_6:1680638-1683125		
J	16	53399	N/A	-0.5791	0.4555	Candidate Polycomb enhancer protein	scaffold_6:262342-264346		
J	16	182845	N/A	-0.6521	0.7317	-	scaffold_6:461196-461572		
J	16	56331	N/A	-0.4127	0.3908	Putative α-1,6-mannosyltransferase subunit (Mnn10)	scaffold_6:922117-923608		
J	16	49123	N/A	-0.5326	0.4031	(H2AV/H2A.Z) - histone 2A variant, involved in chromosome stability, and could through chromatin remodeling steps be involved in transcriptional regulation of selected genes and is preventing the propagation of epigenetic silencing into neighboring euchromatin; H2AV also plays a role in efficient DNA repair; H2AV shows a high degree of conservation withing the fungal kingdom; KOG Class: Chromatin structure and dynamics; KOG Id: 1757; KOG Description: Histone 2A	scaffold_7:1397913-1398767	69	
J	16	53682	N/A	-0.5743	0.5089	mRNA cleavage and polyadenylation factor I complex, subunit RNA15	scaffold_7:1400902-1402852	69	
J	16	210522	N/A	-0.4391	0.3682	-	scaffold_7:448368-448957		
J	16	195354	N/A	-0.3973	0.356	-	scaffold_72:186-1469		
J	16	185623	N/A	-0.5364	0.3797	-	scaffold_8:1575064-1575587		
J	16	49324	N/A	-0.8561	0.6707	Predicted esterase of the α-β hydrolase superfamily	scaffold_8:780502-785205	70	
J	16	41719	N/A	-0.6317	0.55	hypothetical FAD/FMN-containing dehydrogenase	scaffold_8:788271-789930	70	
J	16	185570	N/A	-0.4927	0.5059	Acyl-CoA dehydrogenase, central region	scaffold_8:832990-834263		
J	16	186686	N/A	-0.6595	0.4033	hypothetical dihydrofolate reductase	scaffold_9:1147427-1148203		
J	16	53976	N/A	-0.3159	0.3107	-	scaffold_9:489780-490568		
J	17	35780	N/A	-0.3344	0.2492	-	scaffold_1:1326036-1327443		
J	17	51852	N/A	-0.8526	0.8157	Phox-like	scaffold_1:1620782-1622333		
J	17	171693	N/A	-0.5517	0.4405	-	scaffold_1:1798864-1800251		
J	17	171846	N/A	-1.515	1.0949	hypotheticial alkaline ceramidase	scaffold_1:2025407-2026605		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	17	46645	N/A	-0.6717	0.4214	-	scaffold_1:2322429-2323767		
J	17	170595	N/A	-0.4277	0.414	WD40 associated region in TFIID subunit	scaffold_1:2359053-2361635	71	
J	17	36119	N/A	-0.9271	0.8328	-	scaffold_1:2362163-2362856	71	
J	17	51989	N/A	-0.8072	0.5718	Splicing coactivator	scaffold_1:2882056-2884224		
J	17	46323	N/A	-0.7588	0.5749	-	scaffold_1:536829-538449		
J	17	46347	N/A	-0.4776	0.4424	Transcriptional corepressor	scaffold_1:665476-668305		
J	17	55273	N/A	-0.758	0.6214	ABC transporter protein. Induced at low pH (2.5).	scaffold_1:701072-705858		
J	17	205594	N/A	-1.1866	1.0032	hypothetical. Methionyl aminopeptidase	scaffold_1:954159-955854		
J	17	188031	N/A	-0.8741	0.6064	-	scaffold_10:1687549-1688528		
J	17	202702	N/A	-1.3488	1.2308	putative ER Ca2+ transporting ATPase	scaffold_10:1885199-1888484		
J	17	187240	N/A	-0.4116	0.3767	Iron/ascorbate family oxidoreductases	scaffold_10:409290-410681		
J	17	212654	N/A	-0.6799	0.5218	-	scaffold_11:1106877-1110016		
J	17	50026	N/A	-1.0878	0.7499	-	scaffold_11:180891-181979		
J	17	43230	N/A	-0.4412	0.3561	Hypothetical SNARE protein	scaffold_11:556984-557878		
J	17	212529	N/A	-0.4934	0.4503	-	scaffold_11:668956-670375		
J	17	122116	N/A	-1.361	1.0716	Metacaspase involved in regulation of apoptosis	scaffold_11:704320-705504		
J	17	50631	N/A	-0.4432	0.4106	Hypothetical. Casein kinase II, regulatory subunit domain	scaffold_13:1112731-1113822		
J	17	190360	N/A	-1.0017	0.6474	-	scaffold_13:45452-46798		
J	17	44128	N/A	-0.8615	0.754	-	scaffold_13:473866-475071		
J	17	190225	N/A	-0.8455	0.7532	Putative N2,N2-dimethylguanosine tRNA methyltransferase	scaffold_13:586396-587550		
J	17	213454	N/A	-0.9002	0.7185	ABC transporter	scaffold_14:239602-244793		
J	17	120745	N/A	-0.4081	0.3664	Response regulator receiver	scaffold_14:366792-368510		
J	17	191956	N/A	-1.2287	0.899	related to extracellular aspartic protease	scaffold_15:537782-539363		
J	17	213924	N/A	-0.4972	0.4402	-	scaffold_16:349791-350838		
J	17	119891	N/A	-0.4825	0.5163	Inorganic pyrophosphatase	scaffold_16:372015-374595		
J	17	51044	N/A	-0.5832	0.5205	-	scaffold_16:648890-653379		
J	17	193209	N/A	-0.7512	0.6331	ABC transporter	scaffold_17:127700-130174		
J	17	57395	N/A	-0.8053	0.7242	Glycosyl transferase, family 39	scaffold_18:214405-216852		
J	17	214511	N/A	-0.5346	0.441	Protein kinase	scaffold_18:326894-328110		
J	17	214515	N/A	-0.4818	0.4637	Hypothetical RING finger protein	scaffold_18:337202-339631		
J	17	174468	N/A	-0.504	0.5332	Hypothetical emopamil-binding	scaffold_2:1302147-1302812		
J	17	123805	N/A	-0.8372	0.7141	Predicted seven transmembrane receptor - rhodopsin family	scaffold_2:1454591-1456119		
J	17	174133	N/A	-0.7805	0.5825	Hypothetical phosphatidate cytidylyltransferase	scaffold_2:2652224-2653378		
J	17	37283	N/A	-0.5565	0.4371	Phosphoribosylformylglycinamidine synthase	scaffold_2:2823643-2827447		
J	17	37617	N/A	-0.5728	0.4762	Riboflavin kinase / FAD synthetase	scaffold_2:3910977-3911735		
J	17	52494	N/A	-0.9348	0.911	-	scaffold_2:3962145-3963337		
J	17	173352	N/A	-0.7112	0.5111	DnaJ related protein	scaffold_2:521015-522048		
J	17	52144	N/A	-0.4239	0.3396	Vacuolar H+-ATPase V1 sector	scaffold_2:528747-530747	72	
J	17	118704	N/A	-0.407	0.4059	Predicted GYF domain protein	scaffold_2:530959-537714	72	
J	17	57446	N/A	-0.3057	0.2721	Peptidase M24	scaffold_20:161978-163698		
J	17	194715	N/A	-0.5321	0.4707	putative calcium-dependent, mannose-binding lectin implicated in substrate-specific glycoprotein secreting pathway	scaffold_20:170671-172250		
J	17	130509	N/A	-0.9421	0.7903	Protein kinase	scaffold_20:235381-237693		
J	17	55184	N/A	-1.0249	0.6919	-	scaffold_21:137006-138178		
J	17	138839	N/A	-1.3319	1.3137	Hypothetical cation transporting ATPase	scaffold_24:110998-114174		
J	17	207862	N/A	-0.5597	0.41	This domain is found in a number of fungal transcription factors. The N-terminal region of a number of fungal transcriptional regulatory proteins contains a Cys-rich motif that is involved in zinc-dependent binding of DNA.	scaffold_3:1655506-1657287		
J	17	207864	N/A	-0.4302	0.4201	Synaptobrevin/VAMP-like protein	scaffold_3:1663324-1664190		
J	17	55755	N/A	-0.3224	0.2819	-	scaffold_3:1896287-1897194		
J	17	207992	N/A	-0.8201	0.5997	Hypothetical phosphoinositide-specific phospholipase C	scaffold_3:1944622-1948092		
J	17	207997	N/A	-0.5978	0.4983	Hypothetical protein with copper fist DNA-binding	scaffold_3:1979754-1981511		
J	17	47533	N/A	-0.8051	0.6544	Amino acid permease	scaffold_3:2258962-2260663		
J	17	208206	N/A	-0.5928	0.5525	Hypothetical, contains 14-3-3- like domain	scaffold_3:2743094-2744173		
J	17	38489	N/A	-0.5223	0.4406	hypothetical protein; KOG Class: Transcription; KOG Id: 0870; KOG description: DNA polymerase epsilon, subunit D	scaffold_3:3007527-3008481		
J	17	208393	N/A	-0.5505	0.5793	Helix loop helix transcription factor EB	scaffold_3:3298177-3299652		
J	17	198943	N/A	-0.6005	0.5899	Phosphorylcholine transferase/cholinephosphate cytidylyltransferase	scaffold_3:3431880-3433479		
J	17	207656	N/A	-0.6901	0.6168	Hypothetical serine palmitoyltransferase	scaffold_3:629674-631369		
J	17	208884	N/A	-0.423	0.408	NADH-ubiquinone oxidoreductase,	scaffold_4:1616666-1617654		
J	17	208535	N/A	-0.9301	0.7449	-	scaffold_4:165831-166981		
J	17	178361	N/A	-0.7406	0.6361	-	scaffold_4:205651-207060		
J	17	53046	N/A	-0.7947	0.6339	hypothetical protein containing fungal specific transcription factor domain.	scaffold_4:2450609-2452914		
J	17	209050	N/A	-0.4286	0.4067	Radical SAM superfamily	scaffold_4:2508851-2510101		
J	17	55959	N/A	-0.7507	0.5342	-	scaffold_4:780903-782270		
J	17	200100	N/A	-0.5831	0.4094	-	scaffold_5:1141103-1142731		
J	17	39962	N/A	-0.7526	0.7365	Phosphoinositide 3-kinase, C2	scaffold_5:1341469-1344241		
J	17	56125	N/A	-0.4853	0.494	Fructosamine kinase	scaffold_5:201045-202140		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	17	180585	N/A	-0.5359	0.5332	Predicted membrane proteins, contain hemolysin III domain	scaffold_5:287209-288767		
J	17	209234	N/A	-0.4419	0.3448	-	scaffold_5:36442-36594		
J	17	129525	N/A	-0.8997	0.71	Predicted DHHC-type Zn-finger protein	scaffold_6:1748520-1752377		
J	17	182870	N/A	-0.4197	0.4325	Related to A. fumigatus N,N-dimethylglycine oxidase (EC 1.5.99.2)	scaffold_6:763584-765659		
J	17	48748	N/A	-0.603	0.5672	Type I phosphodiesterase/nucleotide pyrophosphatase	scaffold_6:960340-962576		
J	17	49158	N/A	-1.2039	0.848	Hypothetical NADH:flavin oxidoreductase/NADH oxidase-like protein	scaffold_7:1618331-1619662		
J	17	40966	N/A	-0.8033	0.626	Cu/Zn Superoixide dismutase	scaffold_7:229120-230030		
J	17	41873	N/A	-0.4772	0.5022	Hypothetical protein. RRM motif-containing protein	scaffold_8:1272948-1274948	73	
J	17	201712	N/A	-0.7143	0.6855	-	scaffold_8:1275935-1276683	73	
J	17	201784	N/A	-0.7357	0.6049	Hypothetical N-acetylglucosaminyl phosphatidylinositol de-N-acetylase	scaffold_8:1590774-1591752		
J	17	41661	N/A	-0.7562	0.5107	-	scaffold_8:616996-617907		
J	17	211108	N/A	-0.7202	0.6128	putative CaaX Prenyl protein protease	scaffold_8:874233-875431		
J	17	186415	N/A	-1.0757	0.9269	Short-chain dehydrogenase/reductase	scaffold_9:426520-427591		
J	18	51824	N/A	-0.6455	0.7147	(treB) intracellular GH family 37 neutral trehalase; its homologue in Aspergillus nidulans is not induced by heat shock but induced upon heat shock recovery	scaffold_1:1403480-1405946		
J	18	35970	N/A	-0.7537	0.7189	Predicted component of DNA replication checkpoint response mechanism (S-M checkpoint)	scaffold_1:1912117-1912807		
J	18	36079	N/A	-0.8871	0.8383	-	scaffold_1:2224692-2225921		
J	18	206051	N/A	-0.3456	0.3167	6-phosphogluconolactonase - like protein	scaffold_1:2397392-2398192		
J	18	172591	N/A	-0.8729	0.9032	Uroporphyrinogen decarboxylase	scaffold_1:2791101-2792394		
J	18	196788	N/A	-0.4918	0.4869	hypothetical CCAAT-binding factor; KOG Class: Transcription; KOG Id: 0869; KOG description: CCAAT-binding factor, subunit A (HAP3)	scaffold_1:3213046-3214244		
J	18	171198	N/A	-0.4881	0.5196	-	scaffold_1:3244768-3246327		
J	18	36517	N/A	-0.7413	0.7773	-	scaffold_1:3815663-3816100		
J	18	205471	N/A	-0.7467	0.76	putative Xaa-Pro dipeptidase	scaffold_1:526060-527634		
J	18	171388	N/A	-0.7793	0.7572	Predicted regulator of the ubiquitin pathway (contains UAS and UBX domains)	scaffold_1:708346-709954		
J	18	171507	N/A	-0.4821	0.4754	Related to S. pombe Histidinol-phosphate aminotransferase (EC 2.6.1.9)	scaffold_1:817490-818926		
J	18	187475	N/A	-0.685	0.6856	-	scaffold_10:1133810-1134733		
J	18	211948	N/A	-0.9957	0.9911	Protein kinase	scaffold_10:743290-745415		
J	18	56791	N/A	-0.5119	0.5384	Fungal transcriptional regulatory protein	scaffold_10:953121-955803		
J	18	212936	N/A	-0.9313	0.8958	short chain dehydrogenase	scaffold_12:920660-921606		
J	18	190990	N/A	-0.6801	0.7551	Branched-chain amino acid aminotransferase	scaffold_13:1130939-1132288		
J	18	54613	N/A	-0.6963	0.7679	-	scaffold_13:753798-757393		
J	18	50680	N/A	-0.8263	0.9467	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_14:246667-248688		
J	18	191100	N/A	-0.4276	0.3879	-	scaffold_14:77957-78139		
J	18	57281	N/A	-0.6426	0.6606	Hypothetical sodium/hydrogen exchanger protein	scaffold_16:687151-689665		
J	18	174735	N/A	-0.663	0.7871	Hypothetical snRNP	scaffold_2:1000540-1001307		
J	18	55562	N/A	-0.5264	0.5522	ETC complex I subunit	scaffold_2:1476432-1477264		
J	18	207117	N/A	-0.6801	0.8624	AAA ATPase	scaffold_2:2578896-2580460		
J	18	175387	N/A	-0.7066	0.7679	-	scaffold_2:3018764-3019859		
J	18	207249	N/A	-0.6658	0.6758	Cysteine synthase	scaffold_2:3037135-3038314		
J	18	173834	N/A	-0.5409	0.6005	Haloacid dehalogenase-like hydrolase	scaffold_2:3316475-3317721		
J	18	52489	N/A	-0.451	0.4521	putative extracellular protein	scaffold_2:3916895-3918591		
J	18	36689	N/A	-0.4376	0.4433	Ferredoxin/adrenodoxin reductase	scaffold_2:410948-412684		
J	18	38199	N/A	-0.6308	0.6762	-	scaffold_3:1909076-1910108		
J	18	177222	N/A	-0.8139	0.7867	Hypothetical protein. May be involved in protein-protein interactions due to a predicted TPR-like domain	scaffold_3:3088688-3091132		
J	18	208357	N/A	-0.9256	0.8313	-	scaffold_3:3205379-3206645		
J	18	37921	N/A	-0.616	0.6466	-	scaffold_3:866230-868495		
J	18	52885	N/A	-0.8198	0.9249	Cullin	scaffold_4:488337-491060		
J	18	48397	N/A	-0.839	0.9105	HAD-superfamily hydrolase	scaffold_5:1096262-1097589		
J	18	120955	N/A	-0.6611	0.7236	-	scaffold_5:33836-35985		
J	18	48208	N/A	-0.862	0.9722	-	scaffold_5:7545-8570		
J	18	209541	N/A	-0.3926	0.4416	-	scaffold_5:883478-883985		
J	18	40622	N/A	-0.8151	0.847	-	scaffold_6:1145878-1148141		
J	18	48606	N/A	-0.9408	1.006	Predicted membrane protein	scaffold_6:169439-170193		
J	18	56299	N/A	-0.4421	0.4642	-	scaffold_6:497823-500672		
J	18	182286	N/A	-0.5553	0.5485	Major facilitator superfamily	scaffold_6:560300-562081		
J	18	129349	N/A	-0.4904	0.5379	Glutamine phosphoribosylpyrophosphate amidotransferase	scaffold_6:578081-581834		
J	18	53684	N/A	-0.7672	0.8062	HSF/ETS, DNA-binding	scaffold_7:1416600-1419047		
J	18	184646	N/A	-0.4499	0.5026	-	scaffold_8:988652-991320		
J	18	119993	N/A	-0.8702	0.9067	Hypothetical Mg2+ transporter protein, CorA-like	scaffold_9:1447681-1450513		
J	18	42106	N/A	-0.4049	0.4419	Cytochrome P450	scaffold_9:251160-252861		
J	18	186589	N/A	-0.5006	0.5455	WD domain, G-beta repeat	scaffold_9:419291-423643		
J	19	170105	N/A	-0.7744	0.7345	Ras GTPase	scaffold_1:1271444-1272246		
J	19	170858	N/A	-0.5888	0.4663	Predicted mitochondrial carrier protein	scaffold_1:1825865-1826767		
J	19	196384	N/A	-0.7785	0.6503	-	scaffold_1:1883836-1889288		
J	19	170561	N/A	-0.54	0.4792	-	scaffold_1:196537-199309		
J	19	134215	N/A	-0.7252	0.5455	-	scaffold_1:3028354-3029383		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	19	36284	N/A	-0.3889	0.3333	hypothetical protein containing cytochrome c heme-binding site and Zn-finger, C2H2 type domains	scaffold_1:3141503-3144343		
J	19	171085	N/A	-0.3712	0.343	Actin/actin-like	scaffold_1:3510173-3512315		
J	19	172648	N/A	-0.6671	0.6304	Calcium-binding EF-hand	scaffold_1:3911731-3913383		
J	19	196922	N/A	-0.8003	0.8506	hypothetical transcription initiation factor IIF, α subunit	scaffold_1:3943159-3945481		
J	19	55264	N/A	-0.5098	0.6313	Putative transcriptional repressor	scaffold_1:587158-589323		
J	19	35543	N/A	-0.7745	0.7223	Hypothetical protein (contains WD40 repeats)	scaffold_1:613956-615636		
J	19	35590	N/A	-0.3768	0.3529	Oxidoreductase FAD/NAD(P)-binding	scaffold_1:772369-774070		
J	19	126281	N/A	-0.9058	0.8864	Protein with predicted RNA-binding region RNP-1	scaffold_10:1951755-1952351		
J	19	49989	N/A	-0.744	0.5801	-	scaffold_10:1969244-1971499		
J	19	187622	N/A	-0.2966	0.3007	Hypothetical NADH-dehydrogenase (ubiquinone)	scaffold_10:331407-332696		
J	19	189204	N/A	-0.9547	0.8938	Hypothetical DNA repair protein (RAD4 like)	scaffold_11:1081320-1084420		
J	19	54405	N/A	-1.1496	1.203	putative hydrolase or acyltransferase	scaffold_11:1323714-1324610		
J	19	43250	N/A	-0.7438	0.6204	-	scaffold_11:676364-679858		
J	19	54451	N/A	-0.5901	0.5313	Hypothetical. Interpro: UTP-glucose-1-phosphate uridylyltransferase	scaffold_12:126286-127950		
J	19	119101	N/A	-0.7664	0.7159	Nucleolar GTPase/ATPase p130	scaffold_12:159308-163106		
J	19	212826	N/A	-0.5696	0.4492	-	scaffold_12:197829-198161		
J	19	203208	N/A	-0.8676	0.7387	F1-ATP synthase assembly protein	scaffold_12:36276-37433		
J	19	189582	N/A	-1.1817	1.0842	UMUC-like protein	scaffold_12:512370-514231		
J	19	212996	N/A	-0.6729	0.769	-	scaffold_13:20795-23914		
J	19	190697	N/A	-0.3665	0.4305	-	scaffold_13:317269-317949		
J	19	190965	N/A	-0.4476	0.3933	-	scaffold_13:577408-578547		
J	19	190389	N/A	-0.5704	0.5196	Insulinase-like	scaffold_13:592900-596158		
J	19	213157	N/A	-0.6831	0.5776	DNA polymerase delta, regulatory subunit 55	scaffold_13:603353-605793		
J	19	54609	N/A	-0.5125	0.4703	20S proteasome subunits	scaffold_13:732485-733306		
J	19	54682	N/A	-0.3896	0.4918	-	scaffold_14:110939-111701	74	
J	19	127983	N/A	-0.712	0.6157	Farnesyl cysteine-carboxyl methyltransferase	scaffold_14:111999-112532	74	
J	19	54687	N/A	-0.5718	0.5516	Inositol monophosphatase	scaffold_14:147183-148509		
J	19	125514	N/A	-0.5685	0.4406	RRM motif-containing protein	scaffold_14:346868-347691		
J	19	54756	N/A	-0.653	0.6383	Sortilin and related receptors	scaffold_14:932601-937141		
J	19	45093	N/A	-0.6583	0.4856	-	scaffold_16:434752-437112		
J	19	204683	N/A	-0.9207	0.8862	Small nuclear ribonucleoprotein	scaffold_17:234651-235239		
J	19	214323	N/A	-0.3501	0.3004	hypothetical MOZ/SAS-like, Zn finger-like PHD finger protein; KOG Class: Chromatin structure and dynamics; KOG Id: 2747; KOG description: Histone acetyltransferase (MYST family)	scaffold_17:449894-453352		
J	19	45514	N/A	-0.6761	0.547	Hypothetical G-protein with WD-40 repeat	scaffold_18:244833-246605		
J	19	55082	N/A	-0.775	0.7516	Hypothetical DNA-directed RNA polymerase subunit	scaffold_18:463365-463990		
J	19	46999	N/A	-0.7094	0.4839	Related to prephenate dehydrogenase of Candida albicans	scaffold_2:1526136-1528462		
J	19	197567	N/A	-0.5562	0.5146	candidate vacuolar H+-transporting two-sector ATPase, C subunit	scaffold_2:2363990-2364956		
J	19	52343	N/A	-1.0265	0.915	Hypothetical transcription factor TFIIB	scaffold_2:2518958-2521195		
J	19	37420	N/A	-0.4645	0.4655	-	scaffold_2:3302933-3303835		
J	19	207338	N/A	-0.4591	0.526	-	scaffold_2:3332853-3333476		
J	19	52441	N/A	-0.5347	0.4266	Putative GroEL-like chaperone, ATPase	scaffold_2:3475182-3477106	75	
J	19	52442	N/A	-0.9192	0.8904	AAA ATPase	scaffold_2:3477461-3478955	75	
J	19	207435	N/A	-0.7906	0.7161	-	scaffold_2:3695988-3697638		
J	19	46906	N/A	-0.8891	0.7444	-	scaffold_2:465135-465654		
J	19	52186	N/A	-0.5019	0.4332	Hypothetical β-keto-reductase	scaffold_2:926079-927177		
J	19	173212	N/A	-0.581	0.5333	Hypothetical 6-phosphogluconate dehydrogenase, NAD-binding	scaffold_2:936242-939406		
J	19	206667	N/A	-0.3196	0.337	Related to DNA repair protein Rad4	scaffold_2:949431-951977		
J	19	55795	N/A	-0.6817	0.566	-	scaffold_3:2267468-2269024		
J	19	198787	N/A	-0.4528	0.3876	-	scaffold_3:3014028-3017049	76	
J	19	176923	N/A	-0.6276	0.429	-	scaffold_3:3020442-3021642	76	
J	19	38610	N/A	-0.6457	0.5636	possible Translation initiation factor 2B, β subunit (eIF-2Bbeta/GCD7)	scaffold_3:3404640-3406147		
J	19	198992	N/A	-0.8481	0.7102	Heavy metal transport	scaffold_3:3542395-3542774		
J	19	47301	N/A	-0.8194	0.6334	-	scaffold_3:717021-717815	77	
J	19	176112	N/A	-0.8498	0.7293	hypothetical ubiquitin-specific protease	scaffold_3:719536-720924	77	
J	19	55701	N/A	-0.5031	0.5627	-	scaffold_3:759137-760732		
J	19	39069	N/A	-0.7705	0.6357	-	scaffold_4:1306558-1308078		
J	19	209138	N/A	-0.4788	0.4234	Transcription elongation factor	scaffold_4:2737026-2741506	78	
J	19	209145	N/A	-0.7007	0.6691	Interferon-related protein PC4 like	scaffold_4:2746283-2747854	78	
J	19	119698	N/A	-0.9138	0.8674	hypothetical protein, related to yeast zds family proteins; KOG Class: Chromatin structure and dynamics; KOG Id: 1472; KOG Description:Histone acetyltransferase SAGA/ADA, catalytic subunit PCAF/GCN5 and related proteins	scaffold_4:785163-787843		
J	19	39601	N/A	-0.9537	0.8031	sepB: involved in chromosome segregation and initiation of cytokinesis	scaffold_5:122498-125442		
J	19	179991	N/A	-0.6247	0.4942	-	scaffold_5:1253001-1253730		
J	19	138231	N/A	-0.786	0.5636	hypothetical cytochrome C oxidase assembly protein	scaffold_5:1496013-1496553		
J	19	180304	N/A	-0.5478	0.4537	-	scaffold_5:1619894-1621641		
J	19	56235	N/A	-0.6335	0.5411	Peptidase C50, separase	scaffold_5:1744453-1750698		
J	19	39631	N/A	-0.4182	0.3156	-	scaffold_5:215960-217687		
J	19	133702	N/A	-0.8379	0.7658	Esterase/lipase/thioesterase	scaffold_5:2312340-2313750		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	19	209333	N/A	-0.398	0.3942	Shares amino acid sequence identity with yeast DPH2, a protein required, along with Dph1p, Kti11p, Jji3p, and Dph5p, for synthesis of diphthamide, which is a modified histidine residue of translation elongation factor 2 (Eft1p or Eft2p); may act in a complex with Dph1p and Kti11p.	scaffold_5:266279-267988		
J	19	129592	N/A	-0.7434	0.6746	Fungal specific transcription factor	scaffold_5:295664-298671		
J	19	53172	N/A	-0.5811	0.5106	WD-repeat protein WDR6, WD repeat superfamily	scaffold_5:398474-402045		
J	19	209473	N/A	-0.5165	0.5208	Related to histone deacetylase RpdA	scaffold_5:667443-669688		
J	19	199976	N/A	-0.5484	0.549	RNA binding motif protein	scaffold_5:709493-710105		
J	19	181396	N/A	-0.6752	0.5053	Predicted protein shares limited amino acid sequence identity with the Saccharomyces cerevisiae TPT1 gene product; a tRNA 2′-phosphotransferase which catalyzes the final step in tRNA splicing: the transfer of the 2′-PO(4) from the splice junction to NAD(+) to form ADP-ribose 1″-2″cyclic phosphate and nicotinamide.	scaffold_5:823666-828121		
J	19	180397	N/A	-0.4434	0.3664	-	scaffold_5:889587-890761		
J	19	48378	N/A	-0.3974	0.4227	-	scaffold_5:971392-971952		
J	19	210295	N/A	-0.966	0.6771	SNARE protein TLG1/Syntaxin 6	scaffold_6:1533053-1533835		
J	19	48642	N/A	-0.6831	0.5682	Rap/ran-GTPase-activating protein	scaffold_6:448438-453138		
J	19	182232	N/A	-0.5594	0.5851	-	scaffold_6:469901-476372		
J	19	137999	N/A	-0.731	0.6903	Predicted coiled-coil protein	scaffold_6:496916-497303		
J	19	181774	N/A	-0.6337	0.6249	-	scaffold_6:506387-509790		
J	19	182968	N/A	-0.7409	0.7283	Possibly related to mitotic and DNA damage checkpoint protein hus	scaffold_6:528569-529972		
J	19	183237	N/A	-0.8422	0.8739	Hypothetical. Major facilitator superfamily, Monocarboxylate transporter	scaffold_7:1432126-1433613		
J	19	126136	N/A	-0.804	0.7137	Predicted protein shares amino acid sequence identity to the Saccharomyces cerevisiae TIF35 gene product; subunit of the core complex of translation initiation factor 3(eIF3), which is essential for translation.	scaffold_7:278941-280249		
J	19	53586	N/A	-0.7235	0.5814	-	scaffold_7:411526-413890		
J	19	41061	N/A	-0.5589	0.4962	-	scaffold_7:515135-517462		
J	19	201109	N/A	-0.4607	0.3243	Putative GroEL-like chaperone, ATPase	scaffold_7:785569-787555		
J	19	56468	N/A	-0.489	0.4203	-	scaffold_7:914508-917109		
J	19	211185	N/A	-0.7364	0.575	-	scaffold_8:1155850-1156975		
J	19	132000	N/A	-0.4743	0.4537	Peptidyl-prolyl cis-trans isomerase	scaffold_8:1165428-1167322		
J	19	41490	N/A	-0.8744	0.7457	-	scaffold_8:117310-120983		
J	19	127656	N/A	-0.6931	0.5982	Calcium-binding EF-hand	scaffold_8:1244491-1245125		
J	19	201742	N/A	-0.5112	0.3843	Related to the catalytic epsilon subunit of the translation initiation factor eIF2B, the guanine-nucleotide exchange factor for eIF2; activity subsequently regulated by phosphorylated eIF2.	scaffold_8:1482058-1483149		
J	19	133804	N/A	-0.7044	0.5315	Microfibrillar-associated protein	scaffold_8:1535496-1536809		
J	19	185538	N/A	-0.6829	0.625	hypothetical protein predicted to be a glycine cleavage T-protein and to hold a NUDIX hydrolase domain; GO Desc: aminomethyl transferase activity; GO Id: 4047; Interpro desc: Glycine cleavage T protein (aminomethyl transferase)	scaffold_8:1626897-1631139		
J	19	185012	N/A	-1.0469	0.7718	hypothetical WD-40 repeat protein	scaffold_8:1639588-1640815		
J	19	49276	N/A	-0.7152	0.6237	-	scaffold_8:479322-480635		
J	19	211007	N/A	-0.7406	0.5729	-	scaffold_8:569106-570574		
J	19	41747	N/A	-0.6545	0.5768	Flavin-containing monooxygenase	scaffold_8:876603-878616		
J	19	195378	N/A	-0.758	0.8374	RNA polymerase II transcription initiation/nucleotide excision repair factor	scaffold_88:6585-7904		
J	19	202050	N/A	-0.6384	0.5584	Prohibitin-like protein	scaffold_9:1091827-1092913		
J	19	49671	N/A	-0.5186	0.4862	Hypothetical thiamine monophosphate synthase	scaffold_9:1123948-1125806		
J	19	56726	N/A	-0.6434	0.4985	(pyrG) Orotidine 5′-phosphate decarboxylase	scaffold_9:1369875-1370777		
J	19	56745	N/A	-0.6612	0.6437	-	scaffold_9:1662199-1663289		
J	19	51646	N/A	-0.6365	0.5402	epoxide hydrolase	scaffold_9:170160-171644		
J	20	172165	N/A	-1.1067	1.0149	Peptidase, eukaryotic cysteine peptidase active site	scaffold_1:1441472-1442012		
J	20	172732	N/A	-0.4911	0.5588	-	scaffold_1:215032-216695		
J	20	206096	N/A	-0.768	0.7238	Vacuolar assembly/sorting protein VPS8	scaffold_1:2547755-2552493		
J	20	171849	N/A	-0.7515	0.8638	-	scaffold_1:283516-286329		
J	20	206141	N/A	-0.6018	0.6203	Predicted RNA-binding protein involved in translational regulation	scaffold_1:2852078-2853980		
J	20	195925	N/A	-0.5998	0.5927	Transcription factor containing homeobox and Zn-finger	scaffold_1:321543-324092		
J	20	170591	N/A	-0.6175	0.7864	Related to sna41 protein (A. fumigatus)	scaffold_1:387144-389781		
J	20	205537	N/A	-0.7534	0.7428	hypothetical. Sequence identity with S. cerevisiae LSM7 gene; involved in mRNA decay; possibly involved in processing tRNA, snoRNA, and rRNA.	scaffold_1:716072-716589		
J	20	35667	N/A	-0.5737	0.4919	-	scaffold_1:988525-988842		
J	20	56822	N/A	-0.5168	0.6075	Fungal transcriptional regulatory protein	scaffold_10:1683692-1685777		
J	20	187256	N/A	-0.5204	0.59	Hypothetical phosducin	scaffold_10:423883-424778		
J	20	50057	N/A	-0.425	0.4182	Hypothetical Methylenetetrahydrofolate reductase	scaffold_11:310523-312712		
J	20	189796	N/A	-0.6693	0.786	-	scaffold_12:118076-119080		
J	20	44344	N/A	-0.6951	0.6305	β-1,6-N-acetylglucosaminyltransferase	scaffold_13:1172483-1173891		
J	20	54584	N/A	-0.9517	0.8453	Candidate ornithine decarboxylase (EC 4.1.1.17)	scaffold_13:575607-577024		
J	20	128173	N/A	-0.752	0.761	Longin-like	scaffold_14:442293-442891		
J	20	44698	N/A	-0.4705	0.459	-	scaffold_15:149878-150852		
J	20	44761	N/A	-0.7421	0.7652	-	scaffold_15:336887-338719		
J	20	44775	N/A	-0.6744	0.646	-	scaffold_15:394205-395392		
J	20	45086	N/A	-0.3495	0.4815	ADP-ribosylation factor GTPase activator	scaffold_16:402806-404321		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	20	45156	N/A	-0.6933	0.6934	-	scaffold_16:635237-636155		
J	20	214094	N/A	-0.3558	0.336	Protein kinase	scaffold_16:810079-812716		
J	20	214193	N/A	-0.6556	0.6632	-	scaffold_17:104121-106574		
J	20	214244	N/A	-0.5967	0.5938	hypothetical. Intracellular trafficking OR transcription factor	scaffold_17:203084-205119		
J	20	137213	N/A	-0.6195	0.6212	Protein involved in meiotic recombination/predicted coiled-coil protein	scaffold_17:42813-43484		
J	20	45391	N/A	-0.7634	0.8008	-	scaffold_17:497969-499014		
J	20	45489	N/A	-0.4426	0.4232	-	scaffold_18:162424-164564		
J	20	45506	N/A	-0.6726	0.7134	-	scaffold_18:217313-218221		
J	20	194156	N/A	-0.6599	0.6104	Hypothetical anthranilate synthase	scaffold_19:1080-3527		
J	20	45641	N/A	-0.7989	0.7619	Cytochrome P450	scaffold_19:33507-35141		
J	20	129080	N/A	-0.7337	0.6778	-	scaffold_2:1351066-1354752		
J	20	37006	N/A	-0.5082	0.4733	Transferrin receptor and related proteins containing the protease-associated (PA) domain	scaffold_2:1560622-1563342		
J	20	206933	N/A	-0.4656	0.4309	ER to golgi transport protein	scaffold_2:1722158-1724862		
J	20	134099	N/A	-0.4029	0.5526	Uncharacterized ACR, YagE family COG1723	scaffold_2:1758266-1759616		
J	20	52354	N/A	-0.7395	0.8714	Nucleolar GTPase/ATPase	scaffold_2:2606338-2608313		
J	20	175257	N/A	-0.8286	0.8171	hypothetical protein with predicted MT-A70 and N-6 Adenine-specific DNA methylase; KOG Class: Transcription; KOG Id: 2356; KOG description: Transcriptional activator, adenine-specific DNA methyltransferase	scaffold_2:3759852-3761327		
J	20	55543	N/A	-0.5327	0.5322	Metal-dependent phosphohydrolase, HD region	scaffold_2:954760-955492	79	
J	20	175519	N/A	-0.6006	0.5985	Hypothetical Cobalamin synthesis protein	scaffold_2:958770-960240	79	
J	20	141445	N/A	-0.7134	0.721	-	scaffold_3:1249192-1250437		
J	20	38443	N/A	-0.9278	0.9796	Protein kinase	scaffold_3:2852175-2856337		
J	20	198766	N/A	-0.8141	0.8055	Putative prefoldin chaperone	scaffold_3:2937872-2938626		
J	20	38538	N/A	-0.6393	0.4973	-	scaffold_3:3184010-3184542		
J	20	47747	N/A	-0.8134	0.9732	Regulator of G protein	scaffold_3:3500871-3504686		
J	20	129170	N/A	-0.6657	0.6627	Calcium-binding EF-hand	scaffold_4:1393393-1398002		
J	20	199408	N/A	-0.3084	0.3313	Autophagy protein	scaffold_4:1768490-1769246		
J	20	178892	N/A	-0.6953	0.7335	-	scaffold_4:2565766-2566999		
J	20	209184	N/A	-0.6481	0.6644	Oxysterol-binding protein	scaffold_4:2880478-2882028		
J	20	208615	N/A	-0.4912	0.5573	Permease of the major facilitator superfamily	scaffold_4:447498-453011		
J	20	209711	N/A	-0.5842	0.5487	-	scaffold_5:1568857-1576801		
J	20	209878	N/A	-0.8141	0.7115	Xanthine/uracil permeases family	scaffold_5:2037816-2039556		
J	20	40164	N/A	-0.4048	0.378	-	scaffold_5:2086057-2087388		
J	20	181698	N/A	-0.6206	0.6155	Importin-beta	scaffold_5:2111441-2114765		
J	20	53360	N/A	-1.1046	0.9951	-	scaffold_5:2323632-2324681		
J	20	209331	N/A	-0.5688	0.6051	-	scaffold_5:262822-265329		
J	20	39736	N/A	-0.8386	0.871	Histidine kinase	scaffold_5:616942-620979		
J	20	180937	N/A	-0.3581	0.4348	von Willebrand factor and related coagulation proteins	scaffold_5:679985-683017		
J	20	39770	N/A	-0.8995	0.9229	-	scaffold_5:735690-736388		
J	20	128909	N/A	-0.6166	0.5362	-	scaffold_6:156605-161951		
J	20	126969	N/A	-0.5189	0.5483	CDP-alcohol phosphatidyltransferase/Phosphatidylglycerol-phosphate synthase	scaffold_6:291870-292980		
J	20	181821	N/A	-0.6072	0.7316	-	scaffold_6:420142-420663		
J	20	119631	N/A	-0.7909	0.7608	hypothetical translation repression protein	scaffold_6:426481-429345		
J	20	134128	N/A	-0.3616	0.3714	-	scaffold_7:423682-424996	80	
J	20	48971	N/A	-0.7713	0.6953	-	scaffold_7:426718-427683	80	
J	20	210584	N/A	-0.4208	0.4687	Hypothetical electron transfer flavoprotein-ubiquinone oxidoreductase	scaffold_7:585309-587369		
J	20	41118	N/A	-0.5133	0.5422	-	scaffold_7:708384-708873		
J	20	120044	N/A	-0.6392	0.7188	Related to A. nidulans and A. fumigatus palH (a pH-response regulator)	scaffold_8:1132624-1135005		
J	20	184712	N/A	-0.6039	0.6403	-	scaffold_8:1167886-1170114		
J	20	41958	N/A	-0.5749	0.5617	Transport protein particle (TRAPP) complex subunit	scaffold_8:1534012-1534857		
J	20	135497	N/A	-0.7979	0.7011	Alanine racemase	scaffold_8:155702-156502		
J	20	49223	N/A	-0.8698	0.8221	Candidate chitin synthase	scaffold_8:191833-195551		
J	20	211011	N/A	-0.4129	0.4852	-	scaffold_8:580662-581810		
J	20	211078	N/A	-0.6899	0.6439	Actin/actin-like	scaffold_8:807540-810033		
J	20	211551	N/A	-0.8703	0.9767	-	scaffold_9:1032405-1035157		
J	20	54021	N/A	-0.4393	0.4841	-	scaffold_9:1237156-1242028		
J	20	42457	N/A	-0.72	0.7232	Candidate bimA	scaffold_9:1294584-1297231	81	
J	20	54027	N/A	-0.5205	0.5167	Hypothetical pyridoxin synthesis protein/ Imidazoleglycerol-phosphate synthase subunit H-like	scaffold_9:1300795-1301680	81	
J	20	201957	N/A	-0.6715	0.6035	Synaptobrevin/VAMP-like protein	scaffold_9:477688-478352		
J	21	51887	N/A	-1.0823	0.8961	-	scaffold_1:1909380-1910288		
J	21	51934	N/A	-0.7276	0.6444	RuvB-like helicase 2	scaffold_1:2245215-2246743		
J	21	196588	N/A	-0.8405	0.6826	Eukaryotic-type DNA primase,	scaffold_1:2504106-2505711		
J	21	196672	N/A	-0.8565	0.8272	Dynein light chain	scaffold_1:2927456-2928040		
J	21	171671	N/A	-0.7615	0.7283	Ubiquitin-conjugating enzymes	scaffold_1:326259-327276		
J	21	206304	N/A	-0.6557	0.6412	Hypothetical RAS GTPase	scaffold_1:3276654-3277579		
J	21	36567	N/A	-0.9647	0.8631	Predicted α/β hydrolase	scaffold_1:3953581-3956797		
J	21	212120	N/A	-0.5752	0.5779	Phosphoglucomutase/phosphomannomutase	scaffold_10:1205402-1207416		
J	21	202623	N/A	-0.7231	0.6348	Hypothetical protein containing a Golgi phosphoprotein 3 domain	scaffold_10:1720580-1721880		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	21	54428	N/A	-0.7814	0.7319	-	scaffold_11:1649234-1650174		
J	21	56889	N/A	-0.9473	0.896	hypothetical TAF11 protein with predicted histone fold; KOG Class: Transcription; KOG Id: 3219; KOG description: Transcription initiation factor TFIID, subunit TAF11	scaffold_11:270301-271307		
J	21	125515	N/A	-0.8143	0.836	-	scaffold_11:285120-285989		
J	21	212484	N/A	-0.9439	0.7719	hypothetical G-protein β WD-40 repeat protein; KOG Class: Chromatin structure and dynamics; KOG Id: 0264; KOG description: Nucleosome remodeling factor, subunit CAF1/NURF55/MSI1	scaffold_11:452261-453845		
J	21	54358	N/A	-0.697	0.5856	-	scaffold_11:765120-766160		
J	21	54664	N/A	-0.6615	0.5415	G-like protein containing WD-40 repeat	scaffold_13:1148757-1150053		
J	21	213377	N/A	-0.8376	0.7415	-	scaffold_13:1167460-1169822		
J	21	54580	N/A	-1.0107	0.9246	hypothetical folylpolyglutamate synthetase	scaffold_13:558256-559963		
J	21	204025	N/A	-0.7337	0.718	hypothetical methyl transferase	scaffold_14:733385-734979		
J	21	44648	N/A	-0.763	0.777	UDP-N-acetylglucosamine transporter	scaffold_14:956147-957454		
J	21	50833	N/A	-0.9045	0.9392	-	scaffold_15:189423-189988		
J	21	214017	N/A	-0.5891	0.672	MEKK and related serine/threonine protein kinases	scaffold_16:617302-620185		
J	21	57286	N/A	-0.6252	0.5336	RFX family transcription factor	scaffold_16:722019-724683		
J	21	54934	N/A	-0.8103	0.6027	-	scaffold_16:852008-853674		
J	21	54966	N/A	-0.5595	0.3956	-	scaffold_17:123700-125230		
J	21	51185	N/A	-0.8681	0.691	-	scaffold_17:422912-424095		
J	21	45379	N/A	-1.1955	0.9794	N-acetyltransferase	scaffold_17:454757-455852		
J	21	204865	N/A	-1.0093	0.9825	-	scaffold_18:31436-32106		
J	21	214620	N/A	-0.8859	0.8287	Predicted dinucleotide-utilizing enzyme involved in molybdopterin and thiamine biosynthesis	scaffold_19:21050-22696		
J	21	133158	N/A	-0.733	0.5777	Fungal transcriptional regulatory protein	scaffold_2:1805287-1807073		
J	21	197622	N/A	-0.6825	0.57	Putative GroEL-like chaperone, ATPase	scaffold_2:2584404-2586347		
J	21	174977	N/A	-0.4931	0.5155	-	scaffold_2:2682453-2684344		
J	21	175112	N/A	-0.6217	0.5525	-	scaffold_2:3139827-3140557		
J	21	52120	N/A	-0.3918	0.3029	-	scaffold_2:314943-317203		
J	21	37409	N/A	-0.404	0.386	-	scaffold_2:3259125-3260093		
J	21	207437	N/A	-0.5623	0.5641	Myb, DNA-binding	scaffold_2:3698957-3701847		
J	21	206475	N/A	-0.5834	0.5498	-	scaffold_2:408237-410484		
J	21	52127	N/A	-0.8554	0.7032	NSF attachment protein	scaffold_2:427693-428822		
J	21	46917	N/A	-0.6547	0.6124	-	scaffold_2:566125-566828		
J	21	206657	N/A	-0.9211	0.8097	BAR	scaffold_2:906142-907288		
J	21	205183	N/A	-0.6503	0.6422	AAA+-type ATPase	scaffold_20:75667-78443		
J	21	55194	N/A	-1.0917	0.9328	-	scaffold_21:243842-244799		
J	21	207990	N/A	-0.7403	0.7706	Hypothetical Vesicle coat complex COPI, epsilon subunit	scaffold_3:1942240-1943322		
J	21	52668	N/A	-0.6756	0.6933	(trpC) Anthranilate synthase. Trifunctional enzyme bearing the Gln amidotransferase (GATase) domain of anthranilate synthase, indole-glycerolphosphate synthase, and phosphoribosylanthranilate isomerase activities	scaffold_3:2014337-2016649		
J	21	47560	N/A	-0.4987	0.5581	hypothetical protein containing helix-turn-helix, AraC type domain	scaffold_3:2566001-2567109		
J	21	176096	N/A	-0.5495	0.421	-	scaffold_3:3032862-3033244		
J	21	207705	N/A	-0.8918	0.911	Hypothetical 26S proteasome, regulatory subunit	scaffold_3:738712-739984		
J	21	119551	N/A	-0.7053	0.5908	Microtubule-associated protein	scaffold_3:790628-793575		
J	21	39213	N/A	-0.7261	0.6097	-	scaffold_4:1743823-1745053		
J	21	39320	N/A	-0.3968	0.3094	-	scaffold_4:2137401-2138048		
J	21	138229	N/A	-0.5399	0.4864	-	scaffold_4:2555567-2556263		
J	21	209178	N/A	-0.8403	0.8896	Protein kinase	scaffold_4:2873266-2874961		
J	21	209195	N/A	-0.9361	0.7653	Peptidase	scaffold_4:2899283-2901047		
J	21	40039	N/A	-0.9309	0.8799	Peptidase, eukaryotic cysteine peptidase active site	scaffold_5:1637631-1641554		
J	21	180621	N/A	-0.7251	0.5893	Hypothetical protein associated with vesicle transport (v-SNARE)	scaffold_5:1978144-1978848		
J	21	53120	N/A	-0.9169	0.8476	(pmtA) Dolichyl-phosphate-mannose–protein O-mannosyl transferase	scaffold_5:20504-23001		
J	21	48531	N/A	-0.7336	0.7051	Calcium-binding EF-hand	scaffold_5:2101635-2102252		
J	21	48268	N/A	-0.9775	0.9527	Hypothetical aminotransferase. FPrintScan queries indicates aromatic amino acid activity	scaffold_5:310851-312197		
J	21	209236	N/A	-0.7526	0.6715	Ribonuclease HII	scaffold_5:45338-46396		
J	21	200521	N/A	-1.0363	1.0978	-	scaffold_6:277686-278680		
J	21	48724	N/A	-1.1193	1.006	Isocitrate lyase	scaffold_6:852866-854010		
J	21	210788	N/A	-0.7474	0.6045	-	scaffold_7:1627892-1628704		
J	21	200914	N/A	-0.5706	0.5928	Predicted GTPase-activating protein	scaffold_7:254749-256429		
J	21	56424	N/A	-0.678	0.6991	Hypothetical dolichyl-phosphate β-D-mannosyltransferase; belongs to glycosyltransferase 2 family.	scaffold_7:468315-469125		
J	21	183181	N/A	-0.5075	0.4629	Amino acid/polyamine transporter	scaffold_7:493191-495066		
J	21	49007	N/A	-0.6409	0.7301	Dihydropteroate synthase/7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase/Dihydroneopterin aldolase	scaffold_7:594554-595679		
J	21	41454	N/A	-0.4914	0.4599	-	scaffold_8:12093-12939		
J	21	41890	N/A	-0.6751	0.5352	Ras-related small GTPase	scaffold_8:1324673-1325646		
J	21	184554	N/A	-0.9773	0.8903	Hypothetical. KOG suggests iron transporter activity	scaffold_8:1504101-1505880		
J	21	41629	N/A	-0.51	0.4716	-	scaffold_8:536483-537700		
J	21	41759	N/A	-0.5447	0.5666	-	scaffold_8:916555-917343		
J	21	49696	N/A	-0.4683	0.4227	Longin-like	scaffold_9:1255963-1256626		
J	21	211641	N/A	-0.5396	0.4181	-	scaffold_9:1310309-1311006		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	21	56669	N/A	-0.5963	0.5611	DEAD/DEAH box helicase	scaffold_9:371752-373824		
J	22	46481	N/A	-0.7954	0.7412	Actin/actin-like	scaffold_1:1442960-1444228		
J	22	171764	N/A	-0.7543	0.7135	-	scaffold_1:1524971-1525684		
J	22	35944	N/A	-0.665	0.7812	hypothetical nitrilase-like protein	scaffold_1:1850702-1851797		
J	22	46576	N/A	-0.832	0.7689	Hypothetical protein with Zn-finger	scaffold_1:1922179-1922955		
J	22	172685	N/A	-0.7833	0.8478	-	scaffold_1:2452751-2454166		
J	22	170718	N/A	-0.7752	0.8121	Hypothetical protein with calcium-binding EF-hand domain	scaffold_1:3156107-3157039		
J	22	206262	N/A	-0.422	0.4408	Shares amino acid sequence identity with Saccharomyces cerevisiae FUN12 gene product comprising a GTPase required for general translation initiation by promoting Met-tRNAiMet binding to ribosomes and ribosomal subunit joining	scaffold_1:3164791-3168118		
J	22	171497	N/A	-0.7863	0.7214	Short-chain dehydrogenase/reductase	scaffold_1:3690834-3691815		
J	22	36571	N/A	-0.8796	0.8329	-	scaffold_1:3968706-3969980		
J	22	171648	N/A	-0.4754	0.5062	-	scaffold_1:411884-413230	82	
J	22	171583	N/A	-0.766	0.7358	-	scaffold_1:413609-414223	82	
J	22	35566	N/A	-0.7795	0.8819	Short-chain dehydrogenase/reductase	scaffold_1:694333-695338		
J	22	171394	N/A	-0.6205	0.5713	Fe-S oxidoreductase	scaffold_1:870470-872638		
J	22	187222	N/A	-0.711	0.7958	PpiC-type peptidyl-prolyl cis-trans isomerase	scaffold_10:1018365-1019061		
J	22	187292	N/A	-0.7244	0.656	Alcohol dehydrogenase	scaffold_10:1086480-1087551		
J	22	42921	N/A	-0.9703	0.983	-	scaffold_10:1156727-1157396		
J	22	212124	N/A	-1.067	1.0351	Hypothetical protein with Per1-like domain (involved in homeostasis)	scaffold_10:1207996-1209170		
J	22	187422	N/A	-0.5951	0.7359	-	scaffold_10:1712034-1712739		
J	22	54260	N/A	-0.7087	0.741	Hypothetical 20S proteasome, regulatory subunit	scaffold_10:1966867-1967705		
J	22	143709	N/A	-0.9038	0.7074	-	scaffold_10:1999382-1999825		
J	22	211926	N/A	-0.5202	0.5425	Hypothetical protein methyltransferase	scaffold_10:714522-717264		
J	22	128523	N/A	-0.5463	0.575	Mitochondrial ribosomal protein S27	scaffold_11:1121-1516		
J	22	202783	N/A	-0.6334	0.623	Ras small GTPase,	scaffold_11:40409-41284		
J	22	212502	N/A	-0.619	0.5619	Hypothetical nucleosome assembly protein	scaffold_11:555673-556924		
J	22	56861	N/A	-0.6755	0.7862	candidate ER lumen protein retaining receptor	scaffold_11:5956-6948		
J	22	188775	N/A	-0.7725	0.7644	Serine/threonine protein kinase	scaffold_11:741811-743293		
J	22	189410	N/A	-0.5331	0.5432	Hypothetical, contains Predicted peptidyl prolyl cis-trans isomerase domain	scaffold_12:128719-130337		
J	22	44351	N/A	-0.8068	0.8277	prenyltransferase activity	scaffold_13:1189048-1190165		
J	22	133377	N/A	-0.4932	0.5863	-	scaffold_13:273022-274606		
J	22	126341	N/A	-0.8959	0.8647	Hypothetical protein with HMG-I and HMG-Y, DNA-binding domains	scaffold_13:348290-349364		
J	22	213140	N/A	-0.8529	0.7364	Putative phosphoinositide phosphatase	scaffold_13:560774-563001	83	
J	22	121177	N/A	-0.4624	0.5321	-	scaffold_13:565522-567500	83	
J	22	54593	N/A	-0.9031	0.8568	Amino acid/polyamine transporter	scaffold_13:629257-631572		
J	22	213187	N/A	-0.6038	0.5611	Vesicle coat protein clathrin,	scaffold_13:647825-653258	84	
J	22	213194	N/A	-0.7037	0.7887	Putative growth response protein	scaffold_13:658795-659905	84	
J	22	203639	N/A	-0.6048	0.6994	ATP-dependent RNA helicase	scaffold_13:662140-668918	84	
J	22	143563	N/A	-0.6835	0.5913	Ribosomal protein	scaffold_13:672935-673561	84	
J	22	57073	N/A	-0.4648	0.4382	proteasome β-subunit	scaffold_13:708904-709772		
J	22	213453	N/A	-0.3926	0.3894	Nuclear protein export factor	scaffold_14:214918-218942		
J	22	213656	N/A	-1.3622	1.4775	C2 domain	scaffold_15:66349-68231		
J	22	57188	N/A	-0.8127	0.7873	RNA polymerase	scaffold_15:82914-84092		
J	22	44995	N/A	-0.6646	0.6626	Hypothetical protein with Zn-finger, Tim10/DDP type	scaffold_16:133191-133704		
J	22	204434	N/A	-0.2978	0.3444	Hypothetical NADH:ubiquinone oxidoreductase 17.2 kD subunit	scaffold_16:583059-583823		
J	22	54938	N/A	-0.527	0.4731	Polypeptide release factor involved in translation termination.	scaffold_16:869972-871484		
J	22	204572	N/A	-0.5729	0.7236	Shares amino acid sequence identity with Saccharomyces cerevisiae FAP7 gene product; an essential NTPase required for small ribosome subunit synthesis; mediates processing of the 20S pre-rRNA at site D in the cytoplasm but associates only transiently with 43S preribosomes via Rps14p.	scaffold_16:890244-890938		
J	22	54952	N/A	-0.7628	0.7012	-	scaffold_16:920188-921107		
J	22	214212	N/A	-0.8647	0.9088	Vesicle coat protein clathrin, light chain	scaffold_17:132812-133768	85	
J	22	54970	N/A	-0.8696	0.9082	-	scaffold_17:134259-135720	85	
J	22	51134	N/A	-0.8302	0.8216	putative transmembrane GH family 47 mannosyl-oligosaccharide 1,2-alpha-mannosidase	scaffold_17:143426-145396		
J	22	54989	N/A	-0.7165	0.6538	-	scaffold_17:301241-303259		
J	22	54997	N/A	-0.897	0.7725	(eaf3) EAF3 chromatin modification related protein	scaffold_17:370673-372036		
J	22	194079	N/A	-0.7305	0.8168	Small nuclear ribonucleoprotein	scaffold_18:367154-367823		
J	22	45562	N/A	-0.673	0.7938	-	scaffold_18:411817-412889		
J	22	193846	N/A	-0.8804	0.8225	Hypothetical peptidyl-prolyl cis-trans isomerase, cyclophilin type	scaffold_18:7546-8427		
J	22	45694	N/A	-0.9816	0.943	-	scaffold_19:183713-184327		
J	22	206769	N/A	-0.7371	0.8855	Predicted E3 ubiquitin ligase	scaffold_2:1309555-1310676		
J	22	207110	N/A	-0.8188	0.9168	Kinesin-like protein	scaffold_2:2558793-2561489		
J	22	52397	N/A	-0.6683	0.7449	Hypothetical 20S proteasome, regulatory subunit	scaffold_2:3048179-3049501		
J	22	52421	N/A	-0.4532	0.3879	Peptidase M18, aminopeptidase I	scaffold_2:3310466-3312227		
J	22	174822	N/A	-0.6043	0.6429	Putative cytochrome C oxidase assembly protein	scaffold_2:3608128-3609179		
J	22	37641	N/A	-0.9648	1.0083	hypothetical TPR-like protein; KOG Class: Chromatin structure and dynamics; KOG Id: 4563; KOG Description: Cell cycle-regulated histone H1-binding protein	scaffold_2:3987515-3988940		
J	22	207543	N/A	-0.6633	0.7522	Hypothetical Nuclear division RFT1 protein	scaffold_2:4008981-4010386		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	22	173627	N/A	-0.7067	0.7985	HypB/UreG, nucleotide-binding	scaffold_2:434566-435530		
J	22	36776	N/A	-0.7335	0.7585	Ras GTPase	scaffold_2:750159-750994		
J	22	176028	N/A	-0.5678	0.6692	-	scaffold_3:1348833-1349804		
J	22	47429	N/A	-0.5009	0.6811	(dphE) Methyltransferase required for synthesis of diphthamide, which is a modified histidine residue of translation elongation factor 2.	scaffold_3:1731489-1732488		
J	22	123165	N/A	-0.8622	1.0159	Predicted GTP-binding protein	scaffold_3:1875988-1877846		
J	22	47458	N/A	-0.543	0.5767	-	scaffold_3:1897550-1898941		
J	22	38222	N/A	-0.7131	0.6027	-	scaffold_3:1982444-1983492		
J	22	198703	N/A	-0.6992	0.7167	Putative cargo transport protein	scaffold_3:2752282-2753171		
J	22	38493	N/A	-0.8457	0.7634	candidate V-Snare	scaffold_3:3019288-3020119		
J	22	52779	N/A	-0.6351	0.6157	-	scaffold_3:3099661-3102253		
J	22	176861	N/A	-0.5031	0.4927	candidate zinc finger protein, C2H2 type domain	scaffold_3:3113097-3114328		
J	22	52785	N/A	-0.5213	0.5056	-	scaffold_3:3156951-3158507		
J	22	47683	N/A	-0.7119	0.8739	-	scaffold_3:3213759-3214587		
J	22	55885	N/A	-0.7209	0.7213	Hypothetical protein with RNA-binding region	scaffold_3:3394375-3395205	86	
J	22	52816	N/A	-0.7544	0.8346	-	scaffold_3:3397249-3398015	86	
J	22	177851	N/A	-0.6524	0.7595	FOG: WD40 repeat	scaffold_3:3548014-3549183		
J	22	177709	N/A	-0.5291	0.6397	-	scaffold_3:652987-653856		
J	22	47288	N/A	-0.6995	0.7143	putative Translation initiation factor 2B, epsilon subunit (eIF-2Bepsilon/GCD6) Translation, ribosomal structure and biogenesis	scaffold_3:667114-669520		
J	22	207718	N/A	-0.7289	0.7284	Zn-finger, U1-like	scaffold_3:776767-777296		
J	22	208805	N/A	-0.8089	0.7655	20S proteasome subunit	scaffold_4:1260315-1261300		
J	22	47971	N/A	-0.7244	0.8439	-	scaffold_4:1314488-1315062		
J	22	179405	N/A	-0.6582	0.7393	Conserved hypothetical ATP binding protein	scaffold_4:182288-183470		
J	22	48110	N/A	-1.0652	1.0109	RNA splicing factor	scaffold_4:2444477-2445910		
J	22	53115	N/A	-0.9648	0.9845	-	scaffold_4:2927204-2929399		
J	22	47867	N/A	-0.7342	0.7905	hypothetical CHROMO domain protein; KOG Class: Chromatin structure and dynamics; KOG Id: 1911; KOG Description: Heterochromatin-associated protein HP1 and related CHROMO domain proteins	scaffold_4:659778-660353		
J	22	53243	N/A	-0.6328	0.6347	-	scaffold_5:1004656-1006059		
J	22	129824	N/A	-0.6229	0.6349	SNARE protein TLG1/Syntaxin 6	scaffold_5:1100242-1103329		
J	22	181543	N/A	-0.841	0.727	-	scaffold_5:1182964-1184977		
J	22	128571	N/A	-0.651	0.6114	-	scaffold_5:1362753-1362929		
J	22	39998	N/A	-0.6494	0.6057	Hypothetical subunit of oligosaccharyltransferase	scaffold_5:1496943-1498512		
J	22	40043	N/A	-0.9281	0.7327	-	scaffold_5:1656274-1657428		
J	22	40088	N/A	-0.8846	0.8309	hypothetical protein with predicted Structure-specific recognition protein (SSRP) domain	scaffold_5:1812393-1815022		
J	22	53154	N/A	-1.0157	0.8703	Nuclear distribution protein NUDC	scaffold_5:261559-262327		
J	22	53163	N/A	-0.3892	0.3201	Hypothetical protein with WD40 domain	scaffold_5:318732-320577		
J	22	209218	N/A	-0.9881	0.9525	-	scaffold_5:5647-7117		
J	22	181700	N/A	-0.8419	0.9342	Hypothetical 26S proteasome, regulatory subunit	scaffold_5:665653-666842		
J	22	40634	N/A	-0.5392	0.6067	BTB/POZ domain	scaffold_6:1176948-1177751		
J	22	53511	N/A	-0.6585	0.5882	Hypothetical phosphatidylethanolamine methyltransferase (EC 2.1.1.17)	scaffold_6:1584694-1587854		
J	22	200493	N/A	-0.5062	0.4941	Imidazoleglycerol-phosphate dehydratase	scaffold_6:193472-194288		
J	22	48569	N/A	-0.575	0.5712	-	scaffold_6:23174-23879		
J	22	40412	N/A	-0.7697	0.8658	Synaptobrevin/VAMP-like protein	scaffold_6:486820-487748		
J	22	53418	N/A	-0.6675	0.6683	-	scaffold_6:565627-566803		
J	22	56312	N/A	-0.7362	0.8602	-	scaffold_6:704120-705230		
J	22	53446	N/A	-0.6685	0.6454	-	scaffold_6:774989-777790		
J	22	200656	N/A	-0.7134	0.6945	Protein kinase	scaffold_6:882005-888214		
J	22	56476	N/A	-0.5886	0.6095	Hypothetical 26S proteasome non-ATPase regulatory subunit	scaffold_7:1300667-1301565		
J	22	210734	N/A	-0.8027	0.7576	hypothetical protein with predicted histone deacetylase domain, which catalyzes the removal of acetyl group of acetylated lysine residues in histones; KOG Class: Chromatin structure and dynamics; KOG Id: 1343; KOG Description: Histone deacetylase complex, catalytic component HDA1	scaffold_7:1388443-1391528		
J	22	41360	N/A	-0.5856	0.5233	-	scaffold_7:1526592-1528967		
J	22	48981	N/A	-0.5041	0.5296	Protein with WD40 domain	scaffold_7:471023-473341		
J	22	41055	N/A	-1.1656	1.0656	Ras small GTPase, Ras type	scaffold_7:501005-501995		
J	22	41104	N/A	-0.668	0.8669	-	scaffold_7:663134-663514		
J	22	49047	N/A	-0.9547	0.9661	-	scaffold_7:791460-792114		
J	22	41151	N/A	-0.8397	1.0455	Hypothetical prefoldin subunit	scaffold_7:814179-814854		
J	22	129554	N/A	-0.4247	0.4379	Translation elongation factor 2	scaffold_8:1212737-1216180		
J	22	41865	N/A	-0.5597	0.5205	Peptidase C19, ubiquitin carboxyl-terminal hydrolase 2	scaffold_8:1242108-1244099		
J	22	41891	N/A	-0.9336	0.9786	-	scaffold_8:1326415-1326985		
J	22	211323	N/A	-0.7193	0.7907	-	scaffold_8:1634649-1636544		
J	22	210827	N/A	-0.7971	0.8376	Hypothetical nucleoporin interacting component	scaffold_8:31667-34986		
J	22	185283	N/A	-0.7389	0.6222	-	scaffold_8:4053-5909		
J	22	184571	N/A	-0.8439	0.9845	Pre-mRNA spilicing factor	scaffold_8:574323-575348		
J	22	56516	N/A	-0.7989	0.7555	hypothetical dehydrogenase	scaffold_8:84297-85494		
J	22	185619	N/A	-0.8528	0.7365	Ribosomal protein	scaffold_8:994470-994949		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	22	49678	N/A	-0.873	0.8266	Predicted protein sequence shares amino acid sequence similarity to the Saccharomyces cerevisiae RRP45 gene product; a protein involved in rRNA processing; component of the exosome 3->5 exonuclease complex.	scaffold_9:1151030-1152029		
J	22	124391	N/A	-0.6606	0.7049	Glutamate 5-kinase	scaffold_9:1626697-1628080		
J	22	136275	N/A	-0.556	0.5219	-	scaffold_9:1638875-1639589		
J	22	201858	N/A	-0.7021	0.726	H+-transporting two-sector ATPase	scaffold_9:217361-218205		
J	22	211423	N/A	-0.5613	0.6212	Actin-related protein	scaffold_9:305834-306608		
J	22	49543	N/A	-0.569	0.5567	Hypothetical phosphoglycerate/bisphosphoglycerate mutase	scaffold_9:374519-375509		
J	22	201959	N/A	-0.7542	0.6465	-	scaffold_9:480510-481002		
J	23	171480	N/A	-0.4204	0.3779	Cys/Met metabolism pyridoxal-phosphate-dependent enzymes	scaffold_1:1240510-1242432		
J	23	128934	N/A	-0.7392	0.7179	Predicted protein shares amino acid sequence similarity to the Saccharomyces cerevisiae TRM11 gene product; the catalytic subunit of an adoMet-dependent tRNA methyltransferase complex (Trm11p-Trm112p), required for the methylation of the guanosine nucleotide at position 10 (m2G10) in tRNAs.	scaffold_1:1873640-1879140		
J	23	36230	N/A	-0.9387	0.9362	Candidate mitochondrial import inner membrane translocase	scaffold_1:2957341-2957743		
J	23	170557	N/A	-0.6355	0.6084	-	scaffold_1:3308118-3309151		
J	23	36448	N/A	-0.9545	0.8043	Protein kinase	scaffold_1:3629973-3630908		
J	23	55496	N/A	-0.8018	0.8006	Hypothetical protein with Zn-finger, C-x8-C-x5-C-x3-H type	scaffold_1:3695115-3695823		
J	23	205440	N/A	-0.4321	0.4853	-	scaffold_1:430834-432632		
J	23	46311	N/A	-0.6329	0.5749	Members of tubulin/FtsZ family	scaffold_1:469743-471522		
J	23	187803	N/A	-0.612	0.624	Hypothetical ribosomal protein	scaffold_10:1077922-1078627		
J	23	56808	N/A	-0.6148	0.6719	putative translation initiation factor related to the eIF-2B α subunit	scaffold_10:1113038-1114165		
J	23	187649	N/A	-0.6003	0.7491	Shares amino acid sequence identity with mitochondrial translation initiation factor 2 (IFM1 gene product) of Saccharomyces cerevisiae and Candida albicans.	scaffold_10:1691177-1694344		
J	23	124206	N/A	-0.7095	0.8145	-	scaffold_10:1919521-1920866		
J	23	43045	N/A	-0.6338	0.714	related to proteasome subunit β-like protein	scaffold_10:1964058-1964964		
J	23	49866	N/A	-0.6507	0.9186	-	scaffold_10:907323-907923		
J	23	43065	N/A	-0.6232	0.6194	Ribonuclease III	scaffold_11:1798-2916		
J	23	56915	N/A	-0.487	0.6163	Predicted methyltransferase	scaffold_11:692538-693460		
J	23	128477	N/A	-0.4635	0.4341	-	scaffold_12:169735-170024		
J	23	54667	N/A	-0.6418	0.6107	Ankyrin repeat	scaffold_13:1176671-1180100		
J	23	50645	N/A	-0.7176	0.6247	-	scaffold_13:1201772-1202556		
J	23	44363	N/A	-0.6647	0.6629	Nup133 nucleoporin	scaffold_13:1211310-1215529		
J	23	44214	N/A	-0.6097	0.6103	Peptidase C19	scaffold_13:706622-708526		
J	23	50675	N/A	-0.4162	0.4222	hypothetical Decapping enzyme complex component	scaffold_14:196917-197930		
J	23	54713	N/A	-0.5626	0.6723	Predicted translation product shares amino acid sequence similarity to the Saccharomyces cerevisiae RIT1 gene product; 2'-O-ribosyl phosphate transferase, modifies the initiator methionine tRNA at position 64 to distinguish it from elongator methionine tRNA.	scaffold_14:338476-340182		
J	23	50787	N/A	-1.097	1.0756	-	scaffold_14:951884-954705		
J	23	54762	N/A	-0.5327	0.6522	Adenosine monophosphate deaminase	scaffold_14:965777-967885		
J	23	192211	N/A	-0.6585	0.7844	-	scaffold_15:155264-156361		
J	23	213634	N/A	-0.6129	0.7237	Vesicle coat complex AP-3, delta subunit	scaffold_15:2838-6041		
J	23	44752	N/A	-0.7698	0.7961	20S proteasome, regulatory subunit β type PSMB6/PSMB9/PRE3	scaffold_15:313701-314634		
J	23	192726	N/A	-0.5945	0.6685	Zn-finger, Tim10/DDP type	scaffold_16:877967-878329	87	
J	23	51095	N/A	-0.8875	1.0059	G10 protein	scaffold_16:878715-879367	87	
J	23	193626	N/A	-0.603	0.6906	Deduced amino acid sequence shares identity with the Saccharomyces cerevisiae RRF1 gene product; mitochondrial ribosome recycling factor, essential for mitochondrial protein synthesis and for the maintenance of the respiratory function of mitochondria.	scaffold_18:21707-22587		
J	23	51231	N/A	-0.4333	0.4274	Related to S. cerevisiae alanyl-tRNA synthase (EC 6.1.1.7)	scaffold_18:3447-7354		
J	23	55047	N/A	-0.6722	0.6324	hypothetical membrane receptor	scaffold_18:43892-45777		
J	23	194089	N/A	-0.6304	0.6939	-	scaffold_19:243072-243996		
J	23	52205	N/A	-1.1417	1.071	Related to replication factor C protein	scaffold_2:1117489-1120910		
J	23	206785	N/A	-0.8591	0.8699	-	scaffold_2:1339867-1340829		
J	23	173146	N/A	-0.6186	0.7155	Hypothetical pre-mRNA splicing protein	scaffold_2:2070667-2071388		
J	23	207071	N/A	-0.3502	0.3567	-	scaffold_2:2365743-2366870		
J	23	37225	N/A	-0.6147	0.6635	Hypothetical Zn-finger, NAD(+) ADP-ribosyltransferase	scaffold_2:2592130-2593587		
J	23	175133	N/A	-0.7717	0.6422	Hypothetical splicing factor 3a, subunit 3	scaffold_2:2962531-2964163		
J	23	37375	N/A	-0.5459	0.6265	-	scaffold_2:3142522-3143026		
J	23	128194	N/A	-0.4414	0.4407	-	scaffold_2:3331800-3332347		
J	23	51606	N/A	-0.4829	0.46	Transcription factor, MADS-box	scaffold_2:3360920-3362951		
J	23	198023	N/A	-0.6312	0.5444	Actin/actin-like	scaffold_2:3963787-3965369		
J	23	122747	N/A	-0.8425	0.863	Ran-binding protein RANBP1 and related RanBD domain proteins	scaffold_2:688510-690079		
J	23	176760	N/A	-0.3916	0.4851	Peptidase	scaffold_3:1254222-1257506		
J	23	55744	N/A	-0.661	0.7156	-	scaffold_3:1771294-1773063		
J	23	55762	N/A	-0.7327	0.7504	-	scaffold_3:1929118-1930373		
J	23	208022	N/A	-0.8335	0.8719	-	scaffold_3:2049817-2050792		
J	23	52714	N/A	-0.6232	0.5946	Vacuolar sorting protein VPS1, dynamin, and related proteins	scaffold_3:2574921-2577799		
J	23	137276	N/A	-0.6968	0.7959	Hypothetical 26S proteasome regulatory complex,	scaffold_3:2947673-2948494		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	23	38526	N/A	-0.4085	0.3308	Cell cycle control protein	scaffold_3:3154447-3156535		
J	23	208463	N/A	-0.4286	0.4101	-	scaffold_3:3461312-3462808		
J	23	175816	N/A	-0.7588	0.7254	-	scaffold_3:3556482-3557390		
J	23	38674	N/A	-0.8056	0.7184	-	scaffold_3:3584989-3585885	88	
J	23	208510	N/A	-0.6499	0.8065	Importin-beta, N-terminal	scaffold_3:3586327-3590216	88	
J	23	47312	N/A	-0.5588	0.533	Kinesin-like protein	scaffold_3:754047-756404		
J	23	55707	N/A	-0.7472	0.7571	Nucleotide-sugar transporter	scaffold_3:818445-819759		
J	23	38981	N/A	-0.7134	0.8668	-	scaffold_4:1028326-1029272		
J	23	38727	N/A	-0.4959	0.4588	-	scaffold_4:180896-182089		
J	23	38742	N/A	-0.8722	1.0202	TPR repeat-containing protein	scaffold_4:215875-216812		
J	23	179063	N/A	-0.7916	0.9328	Zn-finger, C2H2 type	scaffold_4:2929823-2931627		
J	23	47866	N/A	-0.6396	0.5978	Putative GroEL-like chaperone, ATPase	scaffold_4:656729-658817		
J	23	200086	N/A	-0.7997	1.0369	-	scaffold_5:1089278-1090185		
J	23	56203	N/A	-0.8016	0.78	Cell division/GTP binding protein	scaffold_5:1263260-1264815		
J	23	39991	N/A	-0.5657	0.7714	-	scaffold_5:1478963-1480009		
J	23	53311	N/A	-0.5846	0.6116	Longin-like	scaffold_5:1715851-1717693		
J	23	127717	N/A	-0.3963	0.3876	-	scaffold_5:1751035-1751737		
J	23	40145	N/A	-0.9137	0.8759	RecA bacterial DNA recombination protein	scaffold_5:2020372-2022149		
J	23	53177	N/A	-0.5049	0.6653	-	scaffold_5:458302-459333		
J	23	180387	N/A	-0.4418	0.5873	-	scaffold_5:49386-50554		
J	23	209239	N/A	-0.4764	0.5515	-	scaffold_5:69881-71098	89	
J	23	180136	N/A	-0.3272	0.3705	Hypothetical mRNA cleavage and polyadenylation factor I/II complex	scaffold_5:75206-77524	89	
J	23	137836	N/A	-0.5948	0.5233	Ribosomal protein	scaffold_5:884401-885016		
J	23	40813	N/A	-0.5087	0.4697	hypothetical protein containing basic-leucine zipper transcription factor domain	scaffold_6:1733090-1734769		
J	23	182597	N/A	-0.4893	0.5438	Zn-finger transcription factor	scaffold_6:28721-32142		
J	23	56295	N/A	-0.6427	0.6556	Nuclear export receptor CSE1/CAS (importin β superfamily)	scaffold_6:453946-457292		
J	23	200642	N/A	-0.5455	0.49	26S proteasome regulatory complex	scaffold_6:857338-858369		
J	23	209964	N/A	-0.479	0.4888	-	scaffold_6:90331-91920		
J	23	120102	N/A	-0.497	0.5527	-	scaffold_7:248040-250425		
J	23	48964	N/A	-0.9177	1.0127	-	scaffold_7:409881-411188		
J	23	143838	N/A	-0.4225	0.475	-	scaffold_7:681170-681581		
J	23	41794	N/A	-0.7013	0.7474	hypothetical CCAAT-binding factor; KOG Class: Transcription; KOG Id: 1657; KOG description: CCAAT-binding factor, subunit A (HAP5)	scaffold_8:1025890-1026636		
J	23	184631	N/A	-0.7906	0.7853	-	scaffold_8:1475537-1476205		
J	23	41955	N/A	-0.6717	0.6527	-	scaffold_8:1515719-1517125		
J	23	185612	N/A	-0.4182	0.369	DNA-polymerase gamma A	scaffold_8:1571092-1574552		
J	23	53809	N/A	-0.6781	0.6887	-	scaffold_8:811374-811937		
J	23	184611	N/A	-0.6846	0.732	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae URB1 gene product; a nucleolar protein required for the normal accumulation of 25S and 5.8S rRNAs, associated with the 27SA2 pre-ribosomal particle; proposed to be involved in the biogenesis of the 60S ribosomal subunit.	scaffold_8:960340-963882		
J	23	49658	N/A	-0.4898	0.4603	Adenosine/AMP deaminase	scaffold_9:1076395-1077468		
J	23	127027	N/A	-0.5397	0.6426	-	scaffold_9:1149785-1150718		
J	23	49730	N/A	-0.6302	0.6803	-	scaffold_9:1415345-1416406		
J	23	211724	N/A	-0.7373	0.749	Eukaryotic protein kinase domain. Involved in signal transduction	scaffold_9:1629635-1630935		
J	24	205956	N/A	-0.6984	0.938	-	scaffold_1:2148685-2151489		
J	24	36465	N/A	-0.5869	0.7541	hypothetical protein with predicted histone-fold; KOG Class: Transcription; KOG Id: 0871; KOG description: Class 2 transcription repressor NC2, β subunit (Dr1)	scaffold_1:3689313-3690026		
J	24	187754	N/A	-0.9155	1.0786	-	scaffold_10:1031632-1033215		
J	24	212077	N/A	-0.6389	0.9004	Vesicle coat complex AP-3, β subunit	scaffold_10:1103295-1105882		
J	24	42907	N/A	-0.6163	0.8496	-	scaffold_10:1111106-1112678		
J	24	187028	N/A	-0.6627	0.9129	-	scaffold_10:1833555-1835149		
J	24	188103	N/A	-0.5633	0.7189	-	scaffold_10:2000365-2001564		
J	24	49836	N/A	-0.6675	0.8214	TAP42-like protein	scaffold_10:672122-673313		
J	24	188051	N/A	-0.6525	0.7581	Hypothetical protein containing calcium-binding EF-hand	scaffold_10:707144-707828		
J	24	128404	N/A	-0.7343	0.8582	-	scaffold_10:793383-793628		
J	24	212320	N/A	-0.6622	0.8437	-	scaffold_11:24630-26339		
J	24	143961	N/A	-0.7008	0.8974	-	scaffold_11:372673-373100		
J	24	50129	N/A	-0.6028	0.6831	Ubc12 like ubiquitin conjugating enzyme E2	scaffold_11:794271-795103		
J	24	212872	N/A	-0.4655	0.5724	Cytoplasmic mRNA cap binding protein; the eIF4E-cap complex is responsible for mediating cap-dependent mRNA translation via interactions with the translation initiation factor eIF4G.	scaffold_12:379845-380712		
J	24	212902	N/A	-0.9214	1.0427	Hypothetical DnaJ domain protein	scaffold_12:503989-505641		
J	24	43609	N/A	-0.9838	1.2722	-	scaffold_12:97068-97973		
J	24	190721	N/A	-0.5716	0.7238	Putative transcription factor	scaffold_13:1185634-1187974	90	
J	24	138178	N/A	-0.4775	0.5449	Glutaredoxin-related protein	scaffold_13:1191764-1192248	90	
J	24	44220	N/A	-0.4003	0.5224	Mitochondrial inheritance and actin cytoskeleton organization protein	scaffold_13:722531-725842		
J	24	54633	N/A	-0.782	1.0516	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_13:882509-883548		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	24	51056	N/A	-0.8713	1.0147	Hypothetical N-(5'-phospho-D-ribosylformimino)-5-amino-1-(5"-phosphoribosyl)-4- imidazole carboxamide isomerase. (EC 5.3.1.16)	scaffold_16:706095-707130		
J	24	214140	N/A	-0.918	1.0255	Myosin	scaffold_16:892175-897237		
J	24	193056	N/A	-0.8422	1.0335	-	scaffold_16:916407-918281		
J	24	54968	N/A	-0.7731	0.9132	-	scaffold_17:130669-132196		
J	24	57355	N/A	-0.9465	1.1081	-	scaffold_17:469440-470204		
J	24	193227	N/A	-0.5812	0.7159	-	scaffold_17:86245-87315		
J	24	51242	N/A	-0.6822	0.8248	CPSF A subunit	scaffold_18:46361-51036		
J	24	193651	N/A	-0.6692	0.7681	Zn-finger, C-x8-C-x5-C-x3-H type	scaffold_18:518711-520329	91	
J	24	55090	N/A	-0.8187	1.0333	This subunit of TFIIF is required for recruitment of RNA polymerase onto the promoter; this gene is known as "TFG2" in S.cerevisiae	scaffold_18:520751-522097	91	
J	24	194249	N/A	-0.6104	0.7831	-	scaffold_19:363081-363680		
J	24	45633	N/A	-0.7968	0.9989	Putative heterokaryon incompatibility factor	scaffold_19:7688-11442		
J	24	119741	N/A	-0.6097	0.813	Hypothetical Cl- channel, voltage gated	scaffold_2:1085528-1088257		
J	24	46977	N/A	-0.6409	0.8143	-	scaffold_2:1187068-1189857		
J	24	46980	N/A	-0.8722	1.0082	ABC transporter	scaffold_2:1230874-1234715		
J	24	120086	N/A	-0.5822	0.6714	EpsA, Thioredoxin/protein disulfide isomerase	scaffold_2:1477813-1480196		
J	24	52275	N/A	-0.4771	0.6818	-	scaffold_2:1670639-1671999		
J	24	55578	N/A	-0.6555	0.8653	20S proteasome, A and B subunits	scaffold_2:1775229-1776310		
J	24	197473	N/A	-0.5249	0.7148	TFIIF-interacting CTD phosphatases, including NLI-interacting factor	scaffold_2:1813118-1815709		
J	24	37126	N/A	-0.6238	0.6991	-	scaffold_2:1969000-1970148		
J	24	174759	N/A	-0.375	0.6226	Cation efflux family	scaffold_2:2037660-2039367		
J	24	207206	N/A	-0.323	0.3999	Glycosyl transferase, family 15	scaffold_2:2818641-2820036		
J	24	52395	N/A	-0.5458	0.8075	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 2025; KOG description: Chromosome condensation complex Condensin, subunit G	scaffold_2:3038903-3042300		
J	24	125526	N/A	-0.7914	0.9406	-	scaffold_2:3757618-3758581		
J	24	37596	N/A	-0.5293	0.7192	Hypothetical mRNA capping enzyme	scaffold_2:3845607-3846836		
J	24	52497	N/A	-0.7071	0.8413	-	scaffold_2:3980806-3984215		
J	24	128007	N/A	-0.9417	1.0815	Membrane protein involved in organellar division	scaffold_2:565247-565732		
J	24	173666	N/A	-0.3644	0.4421	hypothetical protein	scaffold_2:620778-621757		
J	24	136103	N/A	-0.4769	0.6061	-	scaffold_20:128382-129489		
J	24	45884	N/A	-0.5049	0.6996	-	scaffold_20:144164-148815		
J	24	55169	N/A	-0.3891	0.4839	-	scaffold_20:200787-202458		
J	24	38203	N/A	-0.7962	0.9893	-	scaffold_3:1917361-1918245		
J	24	47618	N/A	-0.6326	0.7344	Protein kinase	scaffold_3:2847854-2848670		
J	24	38673	N/A	-0.6131	0.7442	Hypothetical Shugoshin_N, nuclear.	scaffold_3:3582121-3584464		
J	24	47961	N/A	-0.6106	0.804	Protein containing repeated kelch motifs	scaffold_4:1277592-1279718		
J	24	178388	N/A	-0.7145	0.891	Proteasome α-subunit	scaffold_4:1730098-1731091	92	
J	24	179578	N/A	-0.6789	0.797	FF domain protein	scaffold_4:1731466-1733208	92	
J	24	52861	N/A	-0.718	0.9931	Uncharacterized conserved protein XAP-5	scaffold_4:196622-197845		
J	24	178171	N/A	-0.6852	0.7752	Serine/threonine protein kinase	scaffold_4:2099876-2101138		
J	24	56042	N/A	-0.4698	0.5809	Phox-like	scaffold_4:2410617-2411223		
J	24	179596	N/A	-0.5054	0.6058	Phospholipase D1	scaffold_4:2843712-2849254		
J	24	39889	N/A	-0.535	0.6575	CCR4-NOT transcriptional regulation complex	scaffold_5:1120501-1122493		
J	24	181280	N/A	-0.6748	0.9154	Peptidase	scaffold_5:8795-12187		
J	24	40370	N/A	-0.8172	1.0752	Candidate Calcineurin subint B	scaffold_6:260975-261829		
J	24	210048	N/A	-0.5523	0.6981	-	scaffold_6:287661-288365		
J	24	40409	N/A	-0.7572	0.9183	-	scaffold_6:477810-480170		
J	24	209919	N/A	-0.974	1.1149	Tryptophanyl-tRNA synthetase	scaffold_6:6293-7746		
J	24	40314	N/A	-0.6514	0.8279	-	scaffold_6:92456-93771		
J	24	210508	N/A	-0.7625	1.01	Hypothetical L-kynurenine hydrolase	scaffold_7:415876-417507		
J	24	41070	N/A	-0.8406	1.0338	Centromere-associated protein	scaffold_7:557363-559555		
J	24	184562	N/A	-0.6235	0.8326	-	scaffold_8:1427698-1429833		
J	24	53889	N/A	-0.5493	0.7706	-	scaffold_8:1486725-1487929		
J	24	201304	N/A	-0.8207	0.9939	-	scaffold_8:35463-35955		
J	24	41658	N/A	-0.7727	0.8805	-	scaffold_8:606899-607916		
J	24	41453	N/A	-0.8071	1.0267	AAA ATPase	scaffold_8:9117-11421		
J	24	42383	N/A	-0.6813	0.7665	Longin-like	scaffold_9:1068712-1069390		
J	24	211639	N/A	-0.6835	0.8731	-	scaffold_9:1301831-1302577		
J	24	54056	N/A	-0.8901	0.9695	Hypothetical protein kinase	scaffold_9:1587436-1590697		
J	24	49760	N/A	-0.5506	0.6598	Related to C. albicans cystathionine β-synthase (EC 4.2.1.22)	scaffold_9:1617532-1619321	93	
J	24	211722	N/A	-0.5465	0.6844	Ras GTPase	scaffold_9:1621393-1622465	93	
J	24	186597	N/A	-0.7382	0.9003	-	scaffold_9:1641907-1643412		
J	24	53941	N/A	-0.5733	0.7403	-	scaffold_9:248671-250242		
J	25	35810	N/A	-0.6955	0.7337	DEAD/DEAH box helicase	scaffold_1:1425092-1428741		
J	25	131513	N/A	-0.5105	0.5742	Hypothetical asparagine synthase	scaffold_1:1756213-1758046		
J	25	46267	N/A	-0.7857	0.8238	Transcriptional coactivator	scaffold_1:224957-226844		
J	25	35439	N/A	-0.9036	1.0179	Hypothetical part of the anaphase-promoting complex	scaffold_1:234882-236445		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	25	170443	N/A	-0.6752	0.834	Predicted transporter	scaffold_1:3313309-3315223		
J	25	49934	N/A	-0.4732	0.4469	-	scaffold_10:1248741-1250606		
J	25	54269	N/A	-0.561	0.6401	hypothetical protein with RNA binding region RNP-1 and Nuclear protein SET; KOG Class: Chromatin structure and dynamics; KOG Id: 1080; KOG description: Histone H3 (Lys4) methyltransferase complex, subunit SET1 and related methyltransferases	scaffold_10:1995170-1998836		
J	25	186897	N/A	-0.7054	0.777	AAA ATPase	scaffold_10:652133-665296		
J	25	42818	N/A	-0.3692	0.3262	-	scaffold_10:812320-812792		
J	25	56863	N/A	-0.4391	0.4835	Respiratory-chain NADH dehydrogenase	scaffold_11:21071-23625		
J	25	212446	N/A	-0.3611	0.4916	-	scaffold_11:352086-352939		
J	25	212470	N/A	-0.7025	0.7881	Peptidase C19	scaffold_11:404117-408080		
J	25	136718	N/A	-0.6288	0.6722	Protein kinase	scaffold_11:773888-774721		
J	25	212603	N/A	-0.708	0.7895	-	scaffold_11:913356-914405		
J	25	44149	N/A	-0.6893	0.7313	-	scaffold_13:530087-531985		
J	25	191643	N/A	-0.778	0.9771	-	scaffold_14:413358-414194		
J	25	131516	N/A	-0.6057	0.6983	-	scaffold_15:750785-752699		
J	25	119642	N/A	-0.595	0.8102	Rho GTPase activator	scaffold_16:126669-129848		
J	25	122612	N/A	-0.4652	0.5234	Major facilitator superfamily	scaffold_16:663010-664918		
J	25	214151	N/A	-0.7114	0.9194	Protein kinase	scaffold_16:907328-909324		
J	25	214295	N/A	-1.2808	1.3128	-	scaffold_17:365813-366226		
J	25	139357	N/A	-0.6705	0.7279	-	scaffold_18:120471-122816		
J	25	45528	N/A	-0.6123	0.7488	DNA mismatch repair protein MutS	scaffold_18:302105-305135		
J	25	193773	N/A	-0.8268	1.0468	-	scaffold_18:32293-35521		
J	25	127789	N/A	-0.6041	0.7557	Deduced amino acid sequence shares identity with the Saccharomyces cerevisiae LSM4 gene product; part of heteroheptameric complexes (Lsm2p-7p and either Lsm1p or 8p): cytoplasmic Lsm1p complex involved in mRNA decay; nuclear Lsm8p complex part of U6 snRNP and possibly involved in processing tRNA, snoRNA, and rRNA.	scaffold_2:1061006-1061435		
J	25	52202	N/A	-0.375	0.4065	-	scaffold_2:1078219-1079125		
J	25	36891	N/A	-0.7181	0.6343	-	scaffold_2:1161768-1162622		
J	25	174945	N/A	-0.5799	0.5268	Major facilitator superfamily	scaffold_2:1183060-1184464		
J	25	174348	N/A	-0.6102	0.7793	Hypothetical protein with an ubiquitin-activating enzyme repeat	scaffold_2:1381234-1382726		
J	25	37091	N/A	-0.5593	0.6448	-	scaffold_2:1847815-1850430		
J	25	173989	N/A	-0.5219	0.7303	-	scaffold_2:1977641-1979605		
J	25	175534	N/A	-0.7093	0.8034	Guanine-nucleotide dissociation stimulator	scaffold_2:2409117-2414268		
J	25	174002	N/A	-0.7059	0.7356	ABC transporter	scaffold_2:3298381-3302470		
J	25	37564	N/A	-0.6405	0.6902	-	scaffold_2:3734759-3735793		
J	25	128922	N/A	-0.4675	0.5198	-	scaffold_2:3747675-3752670		
J	25	174251	N/A	-0.9098	0.9519	-	scaffold_2:3799122-3800935		
J	25	36742	N/A	-0.7837	0.8965	DNA mismatch repair protein	scaffold_2:588905-592195		
J	25	177749	N/A	-0.6805	0.7829	hypothetical RNA-processing protein, with HAT helix domain	scaffold_3:1119173-1122762		
J	25	176875	N/A	-0.75	0.9406	Receptor-activated Ca2+-permeable cation channels (STRPC family)	scaffold_3:1667646-1671092		
J	25	47444	N/A	-0.4854	0.5397	-	scaffold_3:1834684-1838089		
J	25	38188	N/A	-0.7801	0.9143	N-methyltransferase	scaffold_3:1878913-1880697		
J	25	38370	N/A	-0.8291	1.0234	AMP-dependent synthetase and ligase	scaffold_3:2619291-2621466		
J	25	38591	N/A	-0.8204	0.8348	GCN5-related N-acetyltransferase	scaffold_3:3354476-3355357		
J	25	52554	N/A	-0.4023	0.4826	Related to Leucyl-tRNA synthetase	scaffold_3:698907-702628		
J	25	47307	N/A	-1.0751	1.0648	Methyltransferases	scaffold_3:740559-741423		
J	25	37941	N/A	-0.3584	0.4254	Protein kinase	scaffold_3:932695-933405		
J	25	56021	N/A	-0.6879	0.9837	Helicase-like transcription factor HLTF/DNA helicase RAD5, DEAD-box superfamily	scaffold_4:1781679-1785140		
J	25	134044	N/A	-0.7861	0.895	DHHC-type Zn-finger proteins	scaffold_4:662945-664254		
J	25	208699	N/A	-0.6264	0.6885	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae RSC9 gene product; one of 15 subunits of the 'Remodel the Structure of Chromatin' (RSC) complex; DNA-binding protein involved in the synthesis of rRNA and in transcriptional repression and activation of genes regulated by the Target of Rapamycin (TOR) pathway.	scaffold_4:747890-750238		
J	25	56197	N/A	-0.5508	0.7075	Shares amino acid sequence identity with S. cerevisiae DTD1, a D-Tyr-tRNA(Tyr) deacylase that functions in protein translation; may affect nonsense suppression via alteration of the protein synthesis machinery; ubiquitous among eukaryotes.	scaffold_5:1123141-1124006		
J	25	181494	N/A	-0.4168	0.4999	-	scaffold_5:1256596-1258521		
J	25	53335	N/A	-0.5795	0.6887	hypothetical protein with Myb and SVIRM domains	scaffold_5:1938262-1940500		
J	25	181053	N/A	-1.2794	1.211	ABC transporter	scaffold_5:756608-759519		
J	25	40332	N/A	-0.4465	0.4966	MED6 mediator	scaffold_6:162293-163400		
J	25	40855	N/A	-0.5414	0.6861	Ribokinase	scaffold_6:1882070-1883095		
J	25	40378	N/A	-0.5757	0.6657	Hypothetical protein with a Myb, DNA-binding domain	scaffold_6:282318-284130		
J	25	40924	N/A	-0.5414	0.5522	-	scaffold_7:89829-91160		
J	25	41811	N/A	-0.826	1.093	Molybdopterin synthase sulfurylase	scaffold_8:1070495-1072081		
J	25	185606	N/A	-0.5565	0.7303	-	scaffold_8:397726-399162		
J	25	185776	N/A	-0.9329	1.0512	Transcriptional coactivator p15	scaffold_9:1655629-1656184		
J	25	186787	N/A	-0.3974	0.4331	-	scaffold_9:237820-239662		
J	25	211420	N/A	-0.6115	0.7628	-	scaffold_9:301171-302402		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	25	137582	N/A	-0.5933	0.6286	RNase P subunit that is not also a subunit of RNase MRP, involved in pre-tRNA processing	scaffold_9:370748-371059		
J	25	42167	N/A	-0.8567	0.9149	-	scaffold_9:439763-440350		
J	26	205706	N/A	-0.5164	0.5746	Protein kinase	scaffold_1:1345962-1347494		
J	26	170688	N/A	-0.8412	1.169	-	scaffold_1:1663778-1664949		
J	26	46527	N/A	-0.6103	0.8301	-	scaffold_1:1678730-1679786		
J	26	171513	N/A	-0.6603	0.8594	GCN5-related N-acetyltransferase	scaffold_1:1691621-1692931		
J	26	51700	N/A	-0.6472	0.7752	Medium subunit of clathrin adaptor complex	scaffold_1:212402-214133		
J	26	46787	N/A	-0.7351	0.8297	Short-chain dehydrogenase/reductase	scaffold_1:3267228-3268283		
J	26	46889	N/A	-0.6812	0.9313	Inositol monophosphatase	scaffold_1:3951928-3953093		
J	26	35492	N/A	-0.7074	0.8573	Acyl-CoA thioesterase	scaffold_1:399233-400502		
J	26	130872	N/A	-0.7146	0.8704	Protein kinase	scaffold_1:710755-713298		
J	26	42881	N/A	-0.3946	0.5363	-	scaffold_10:1036113-1037527		
J	26	211828	N/A	-0.5176	0.6777	tigA, Disulphide isomerase	scaffold_10:405768-406913		
J	26	187714	N/A	-0.7026	0.9359	-	scaffold_10:685265-687454		
J	26	187248	N/A	-0.6724	0.7458	-	scaffold_10:752964-755293		
J	26	50236	N/A	-0.7744	0.9821	Hypothetical Esterase/lipase/thioesterase	scaffold_11:1530964-1531902		
J	26	50029	N/A	-0.539	0.666	-	scaffold_11:197286-197854		
J	26	54362	N/A	-0.4106	0.472	Cytoplasmic tryptophanyl-tRNA synthetase	scaffold_11:802009-803498		
J	26	128321	N/A	-0.672	0.9166	Hypothetical anaphase-promoting complex (APC), subunit	scaffold_12:422713-423153		
J	26	190580	N/A	-0.8515	0.9038	Hypothetical protein prenyltransferase, α subunit	scaffold_13:613712-614862		
J	26	213198	N/A	-0.6607	0.7081	Peptidyl-prolyl cis-trans isomerase	scaffold_13:671495-672477		
J	26	50547	N/A	-0.6374	0.7449	putative Zn Metalloprotease, CaaX prenyl protease	scaffold_13:685341-687026		
J	26	54630	N/A	-0.4457	0.6454	Peptidase	scaffold_13:874742-876474		
J	26	57202	N/A	-0.3985	0.4492	-	scaffold_15:191365-192463		
J	26	213793	N/A	-0.6639	0.8795	candidate succinate-semialdehyde dehydrogenase	scaffold_15:490320-491870		
J	26	54765	N/A	-0.7222	0.7971	-	scaffold_15:7146-8274		
J	26	214072	N/A	-0.5195	0.597	SCF ubiquitin ligase, Skp1 component	scaffold_16:743692-744487		
J	26	214104	N/A	-0.4477	0.5359	Homoserine kinase	scaffold_16:842471-843716		
J	26	214305	N/A	-0.7137	0.8873	Hypothetical Vesicle transport protein (v-SNARE)	scaffold_17:384719-385543		
J	26	51267	N/A	-0.6348	0.7518	Oligosaccharyltransferase subunit	scaffold_18:197078-199654		
J	26	214443	N/A	-1.0052	1.2669	Putative Zinc transporter ZIP, Zn /Fe	scaffold_18:38033-39605		
J	26	51602	N/A	-0.8437	1.0068	-	scaffold_2:1808304-1810000		
J	26	174666	N/A	-0.8029	1.0097	-	scaffold_2:2428281-2429764		
J	26	52115	N/A	-0.4529	0.4869	-	scaffold_2:257087-260014		
J	26	173111	N/A	-0.4891	0.587	Ras small GTPase	scaffold_2:2664249-2665086		
J	26	46895	N/A	-1.0229	1.1359	Predicted panthothenate kinase/uridine kinase-related protein	scaffold_2:270701-271411		
J	26	52371	N/A	-0.5875	0.7032	hypothetical. Glycolipid transfer protein ?	scaffold_2:2741359-2742193		
J	26	37595	N/A	-0.7328	0.9529	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 4140; KOG description: Nuclear protein Ataxin-7	scaffold_2:3843412-3844938		
J	26	51610	N/A	-0.531	0.5318	Putative pdiA Protein disulfide isomerase (prolyl 4-hydroxylase β subunit)	scaffold_2:3974506-3976317		
J	26	52503	N/A	-0.9602	1.1512	Peptidase C19	scaffold_2:4018564-4021198		
J	26	206503	N/A	-0.5456	0.5811	Arginyl-tRNA-protein transferase	scaffold_2:479126-481296		
J	26	52177	N/A	-0.8471	1.0149	Glycosyl transferase family 4	scaffold_2:837119-838676		
J	26	36813	N/A	-0.7317	0.869	H+-transporting two-sector ATPase	scaffold_2:869257-869926		
J	26	55190	N/A	-0.8699	1.0344	-	scaffold_21:227573-228523		
J	26	38291	N/A	-0.6624	0.822	-	scaffold_3:2199495-2204091		
J	26	208323	N/A	-0.6288	0.7481	-	scaffold_3:3097431-3099352		
J	26	177328	N/A	-0.6528	0.7294	HMG box-containing protein	scaffold_3:3188906-3190153		
J	26	47261	N/A	-0.8557	1.1284	related to Beta-1,4-mannosyltransferase	scaffold_3:499036-500550		
J	26	177882	N/A	-0.8939	1.0361	-	scaffold_3:645684-647818		
J	26	207667	N/A	-0.8593	1.1234	Hypothetical RING finger protein with Zn-finger domain	scaffold_3:670984-672702		
J	26	52586	N/A	-0.9917	1.0743	Hypothetical protein with TPR-like domain	scaffold_3:926176-929800		
J	26	39108	N/A	-0.8201	0.7967	Predicted NUDIX hydrolase FGF-2 and related proteins	scaffold_4:1437966-1438589		
J	26	178461	N/A	-0.363	0.4255	Editing needed. This protein is an artificial hybrid of a purine-nucleoside phosphorylase activity and a 6-phosphogluconate dehydrogenase. In the CBS 513.88 annotation, these are annotated as An11g06110 and An11g06120 respectively.	scaffold_4:1596230-1599341		
J	26	55918	N/A	-0.3204	0.4495	Serine/threonine-specific protein phosphatase	scaffold_4:167812-169193		
J	26	178166	N/A	-0.8222	0.8776	-	scaffold_4:1837838-1838605		
J	26	179806	N/A	-0.6937	0.8788	-	scaffold_4:2660697-2661534		
J	26	53099	N/A	-0.8981	0.9335	-	scaffold_4:2850919-2852074		
J	26	53103	N/A	-0.6217	0.8696	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_4:2871926-2872915	94	
J	26	56093	N/A	-1.0353	1.1952	hypothetical non-SMC (structural maintenance of chromosome) condensin subunit, XCAP-D2/Cnd1	scaffold_4:2875821-2879717	94	
J	26	48197	N/A	-0.4956	0.5641	Cys/Met metabolism	scaffold_4:2894435-2897003		
J	26	136079	N/A	-0.5576	0.6713	Hypothetical mitochondrial substrate carrier	scaffold_4:2910741-2912053	95	
J	26	53111	N/A	-0.8363	1.0205	hypothetical protein with predicted TPR-repeats and DnaJ, where DnaJ interacts with the chaperone hsp70-like DnaK protein; KOG Class: Defence mechanisms; KOG Id: 0624; KOG description: dsRNA-activated protein kinase inhibitor P58, contains TPR and DnaJ domains	scaffold_4:2914110-2915744	95	
J	26	38904	N/A	-0.3945	0.5062	Hypothetical glyoxylase	scaffold_4:807493-808670		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	26	53297	N/A	-0.4755	0.5134	-	scaffold_5:1591278-1594153		
J	26	40127	N/A	-0.813	1.0574	Siroheme synthase	scaffold_5:1966355-1967208		
J	26	48560	N/A	-0.5694	0.7775	Glutathione S-transferase	scaffold_5:2327682-2328448		
J	26	209410	N/A	-0.7525	1.0361	-	scaffold_5:489190-490402		
J	26	181655	N/A	-0.7022	0.9184	Shares amino acid sequence identity with S. cerevisiae DOM34 gene product, a probable RNA-binding protein that functions in protein translation to promote G1 progression and differentiation, required for meiotic cell division.	scaffold_5:816114-817471		
J	26	40713	N/A	-0.9791	1.1882	Protein kinase	scaffold_6:1426147-1427659		
J	26	56298	N/A	-0.7672	0.927	Putative mannosyl-oligosaccharide glucosidase, GH family 63	scaffold_6:493538-496382		
J	26	53587	N/A	-0.7655	0.9029	-	scaffold_7:414782-415510		
J	26	56465	N/A	-0.6746	0.8184	-	scaffold_7:882429-884302		
J	26	56469	N/A	-0.3264	0.3869	Hypothetical protein with WD40-like region	scaffold_7:921032-925094		
J	26	184467	N/A	-0.6792	0.8854	-	scaffold_8:1334895-1335998		
J	26	210910	N/A	-0.4575	0.4536	AAA ATPase	scaffold_8:247858-249161	96	
J	26	49234	N/A	-0.9056	0.9715	HMG-I and HMG-Y, DNA-binding	scaffold_8:249565-251234	96	
J	26	210814	N/A	-0.8805	1.0904	Ras-related small GTPase	scaffold_8:7073-7817		
J	26	56576	N/A	-1.0384	1.2487	Hypothetical glutamine synthase	scaffold_8:867613-870340		
J	26	185961	N/A	-0.8209	0.8829	Hypothetical maltose acetyltransferase. Homology to *Bacillus sp.* maltose transacetylase	scaffold_9:1357987-1358823		
J	26	202191	N/A	-0.9793	1.006	Peptidase	scaffold_9:1634498-1636916		
J	26	211738	N/A	-0.6716	0.8995	Hypothetical metal binding, DDHD	scaffold_9:1667746-1670708	97	
J	26	186194	N/A	-1.2302	1.3006	COP9 signalosome, subunit CSN3	scaffold_9:1671284-1673067	97	
J	26	127827	N/A	-0.5116	0.59	Translation initiation factor 1A	scaffold_9:400763-401188		
J	26	131021	N/A	-0.5715	0.5894	Fungal transcriptional regulatory protein	scaffold_9:759381-761696		
J	27	170608	N/A	-0.6357	1.0171	hypothetical PHD zinc finger	scaffold_1:1378013-1379480		
J	27	55354	N/A	-0.572	0.8516	Phox-like	scaffold_1:1649635-1651635		
J	27	35956	N/A	-0.5172	0.8155	-	scaffold_1:1879586-1880374	98	
J	27	205870	N/A	-0.5221	0.781	Ubiquitin-conjugating enzyme	scaffold_1:1882659-1883336	98	
J	27	170835	N/A	-0.4361	0.5919	-	scaffold_1:1889848-1891610		
J	27	205997	N/A	-0.6255	0.9469	Uncharacterized protein involved in protein-protein interaction, contains polyproline-binding GYF domain	scaffold_1:2247062-2248417		
J	27	205396	N/A	-0.485	0.7402	-	scaffold_1:239056-240930		
J	27	35444	N/A	-0.741	1.095	Hypothetical part of the anaphase-promoting complex	scaffold_1:249692-252578		
J	27	55422	N/A	-0.4705	0.6033	related to vesicle coat complex COPII, subunit Sec23/24	scaffold_1:2500676-2503334		
J	27	36289	N/A	-0.6029	0.8018	-	scaffold_1:3152902-3154074		
J	27	206270	N/A	-0.6825	0.892	Hypothetical Signal recognition particle, subunit Srp68	scaffold_1:3176648-3178637		
J	27	172301	N/A	-0.8267	1.2551	-	scaffold_1:3310638-3311577		
J	27	170119	N/A	-0.341	0.525	Pyridoxal-dependent decarboxylase	scaffold_1:3366785-3368500		
J	27	36399	N/A	-0.5032	0.7545	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_1:3489256-3490430		
J	27	171978	N/A	-0.6844	0.8701	FOG: Zn-finger	scaffold_1:3612600-3614372		
J	27	170612	N/A	-0.8475	1.1897	-	scaffold_1:3957562-3958986		
J	27	196058	N/A	-0.6338	0.9809	Transcription factor/CCAAT displacement protein	scaffold_1:727689-730135		
J	27	51769	N/A	-0.5152	0.7082	-	scaffold_1:821496-824182		
J	27	55287	N/A	-0.8239	1.0903	Metallophosphoesterase	scaffold_1:843531-844867		
J	27	56801	N/A	-0.8677	1.3247	-	scaffold_10:1026174-1030058		
J	27	202592	N/A	-0.7722	1.1055	Predicted gamma-butyrobetaine,2-oxoglutarate dioxygenase	scaffold_10:1214803-1215874		
J	27	212230	N/A	-0.6855	0.9813	AAA ATPase	scaffold_10:1874005-1875414		
J	27	187283	N/A	-0.5559	0.809	SNF2-related	scaffold_10:1927327-1930841		
J	27	211906	N/A	-0.4625	0.6421	-	scaffold_10:645029-646438		
J	27	123518	N/A	-0.458	0.7129	Uncharacterized conserved protein, contains WD40 repeats	scaffold_10:700226-701824		
J	27	188878	N/A	-0.6153	0.8595	Flavin-containing monooxygenase	scaffold_11:353141-354670		
J	27	130463	N/A	-0.6278	0.9664	Histone H3 (Lys9) methyltransferase SUV39H1/Clr4, required for transcriptional silencing	scaffold_12:233658-235553		
J	27	189693	N/A	-0.8678	1.249	-	scaffold_12:611-1894		
J	27	44305	N/A	-0.7117	0.9741	-	scaffold_13:1025900-1027130		
J	27	54671	N/A	-1.0217	1.5068	Choline phosphate cytidylyltransferase/Predicted CDP-ethanolamine synthase	scaffold_13:1192666-1194168		
J	27	190484	N/A	-0.8966	1.1979	Acyl transferase region	scaffold_13:1209300-1210334		
J	27	57044	N/A	-0.7515	1.2233	Hypothetical delta 1-pyrroline-5-carboxylate reductase	scaffold_13:485394-486416		
J	27	44174	N/A	-0.6064	0.8266	Myosin-like coiled-coil protein	scaffold_13:597044-598631		
J	27	54605	N/A	-0.7659	1.1201	Predicted Zn2+-dependent endopeptidase, insulinase superfamily	scaffold_13:679310-682582		
J	27	44464	N/A	-0.3646	0.6335	-	scaffold_14:377883-381008	99	
J	27	54719	N/A	-0.7599	0.9917	Protein kinase	scaffold_14:383329-385981	99	
J	27	44637	N/A	-0.7595	1.1513	Hypothetical translation initiation factor	scaffold_14:924645-925570		
J	27	213618	N/A	-0.5246	0.8345	Exocyst subunit - Sec10p	scaffold_14:940837-943584		
J	27	54795	N/A	-0.6111	0.8324	Small nuclear ribonucleoprotein	scaffold_15:200859-201487		
J	27	213652	N/A	-0.7129	1.1176	Protein kinase	scaffold_15:33779-36018		
J	27	204111	N/A	-0.4941	0.8527	hypothetical protein with predicted Barren domain, which is required for chromosome segregation in mitosis; KOG Class: Chromatin structure and dynamics; KOG Id: 2328; KOG Description: Chromosome condensation complex Condensin, subunit H	scaffold_15:93863-96631		
J	27	57253	N/A	-0.4719	0.9283	Ubiquitin-conjugating enzyme	scaffold_16:365317-366177	100	

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	27	213937	N/A	-0.5288	0.7793	26S proteasome subunit	scaffold_16:367159-368738	100	
J	27	129107	N/A	-0.8666	1.1223	Hypothetical protein. Is likely to be involved in protein-protein interaction due to the presence of four TPR repeats.	scaffold_16:579221-582814		
J	27	192901	N/A	-0.4853	0.7489	-	scaffold_16:726203-727487	101	
J	27	134428	N/A	-0.2882	0.5037	MT3/SUMO-activating complex, AOS1/RAD31 component	scaffold_16:728896-730113	101	
J	27	192649	N/A	-0.9569	1.3505	Ras-related GTPase	scaffold_16:914774-915519		
J	27	45320	N/A	-0.8944	1.3729	-	scaffold_17:235844-237203		
J	27	57344	N/A	-0.8647	1.1949	Protein prenyltransferase, α subunit	scaffold_17:360364-361634		
J	27	55002	N/A	-0.6023	0.8231	Hypothetical α-1,6-mannosyltransferase subunit (Mnn11), similarity to GI:66849386(Aspergillus fumigatus Af293).	scaffold_17:392170-393372		
J	27	55027	N/A	-0.6946	1.1486	-	scaffold_17:591454-592505		
J	27	51112	N/A	-0.5991	0.7813	Peptidase family M48	scaffold_17:62906-63720		
J	27	193722	N/A	-0.4752	0.6218	-	scaffold_18:179925-180911		
J	27	45548	N/A	-0.5723	0.7993	TATA binding protein associated factor	scaffold_18:362629-366606		
J	27	193906	N/A	-0.7351	1.0543	-	scaffold_18:471681-472497		
J	27	194534	N/A	-0.6854	1.0288	-	scaffold_19:39132-41312		
J	27	119850	N/A	-0.576	1.028	-	scaffold_2:1163307-1165877		
J	27	206867	N/A	-0.6268	0.7694	Transcription factor TFIIB	scaffold_2:1548865-1549920		
J	27	207003	N/A	-0.3844	0.5289	Lysine-ketoglutarate reductase/saccharopine dehydrogenase	scaffold_2:1882994-1887727		
J	27	207030	N/A	-0.4717	0.8552	hypothetical PHD finger and Zn finger-like protein with a predicted Signalp; KOG Class: Chromatin structure and dynamics ; KOG Id: 1973; KOG description: Chromatin remodeling protein, contains PHD Zn-finger	scaffold_2:1949051-1951513		
J	27	207088	N/A	-0.7566	1.1236	AAA ATPase	scaffold_2:2434448-2436681		
J	27	174644	N/A	-0.652	1.0157	Ubiquitin-conjugating enzymes	scaffold_2:2564046-2564553		
J	27	128213	N/A	-0.7069	0.9219	-	scaffold_2:264356-264878		
J	27	129928	N/A	-0.4833	0.9003	WD40 repeat-containing protein	scaffold_2:2967216-2969751		
J	27	120043	N/A	-0.4932	0.7262	RNA-binding protein RBM5 and related proteins, contain G-patch and RRM domains	scaffold_2:3572202-3574782		
J	27	173798	N/A	-0.4817	0.8318	-	scaffold_2:398202-398733		
J	27	52501	N/A	-0.6703	0.9306	Zinc-containing alcohol dehydrogenase	scaffold_2:4013297-4015745		
J	27	173432	N/A	-0.6717	1.1668	-	scaffold_2:424343-427332		
J	27	51436	N/A	-0.8004	1.2139	-	scaffold_20:203040-205310		
J	27	119417	N/A	-0.57	0.9983	Uso1/p115 like vesicle tethering protein	scaffold_3:1826084-1829909	102	
J	27	52642	N/A	-0.3517	0.6047	candidate Isoleucyl-tRNA synthetase, cytoplasmic	scaffold_3:1830396-1833689	102	
J	27	52645	N/A	-0.5269	0.7726	-	scaffold_3:1861580-1864676		
J	27	52653	N/A	-0.5678	0.8901	Phosphotyrosyl phosphatase activator	scaffold_3:1907250-1908509		
J	27	55763	N/A	-0.664	1.2192	(manA) Mannose-6-phosphate isomerase (EC 5.3.1.8)	scaffold_3:1938379-1940008		
J	27	38226	N/A	-0.7143	1.1855	Related to Geranylgeranyl pyrophosphate synthase	scaffold_3:1990553-1991653	103	
J	27	47479	N/A	-0.6225	1.0601	Predicted MutS-related protein involved in mismatch repair	scaffold_3:1992125-1993174	103	
J	27	52670	N/A	-0.7837	1.0687	Synaptic vesicle protein EHS-1 and related EH domain proteins	scaffold_3:2047898-2049317		
J	27	175597	N/A	-0.4351	0.8533	-	scaffold_3:2148850-2150292		
J	27	47529	N/A	-0.5858	1.1566	-	scaffold_3:2235538-2238036		
J	27	176207	N/A	-0.4227	0.6429	-	scaffold_3:2380622-2380996		
J	27	208209	N/A	-0.6194	1.0837	-	scaffold_3:2749982-2750927		
J	27	55880	N/A	-0.4142	0.5327	Protein kinase	scaffold_3:3348464-3351262		
J	27	47735	N/A	-0.6747	1.1002	Uncharacterized conserved protein predicted to be involved in protein sorting	scaffold_3:3453018-3453844		
J	27	208491	N/A	-0.8028	1.2401	WD40 repeat protein	scaffold_3:3528405-3529796		
J	27	37795	N/A	-0.585	0.8717	-	scaffold_3:453484-453894		
J	27	207694	N/A	-0.4882	0.9545	-	scaffold_3:714376-715954		
J	27	55704	N/A	-0.6168	1.188	(tpsA) trehalose-6-phosphate synthase A	scaffold_3:785783-787609		
J	27	37917	N/A	-0.5038	0.9143	Hypothetical. Interpro suggests Adenosine/AMP deaminase domain	scaffold_3:852682-854405		
J	27	178649	N/A	-0.7122	1.1352	Nucleolar GTPase/ATPase p130	scaffold_4:1317284-1320030		
J	27	39124	N/A	-0.3348	0.5879	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae TGS1 gene product; trimethyl guanosine synthase, conserved nucleolar methyl transferase responsible for conversion of the m(7)G cap structure of snRNAs and snoRNAs to m(2,2,7)G; also required for ribosome synthesis and nucleolar morphology.	scaffold_4:1490833-1491735		
J	27	123981	N/A	-0.497	0.8201	-	scaffold_4:1978581-1979951		
J	27	199512	N/A	-0.5762	1.0243	Hypothetical proteasome component	scaffold_4:2467419-2469103		
J	27	119390	N/A	-0.6792	1.0056	Hypothetical vacuolar assembly/sorting protein PEP5/VPS11	scaffold_4:287372-290603		
J	27	179192	N/A	-0.5946	0.8987	Ras small GTPase, Ras type	scaffold_4:778148-780043		
J	27	38927	N/A	-0.56	1.1039	-	scaffold_4:870862-871885		
J	27	47908	N/A	-0.7759	1.2475	Short-chain dehydrogenase/reductase SDR	scaffold_4:892014-893065		
J	27	39944	N/A	-0.4747	0.701	Protein kinase	scaffold_5:1277305-1278657		
J	27	48454	N/A	-0.7112	1.2946	Hypothetical protein. May be involved in sister chromatid cohesion during DNA replication	scaffold_5:1509116-1511128		
J	27	209750	N/A	-0.7482	1.0496	-	scaffold_5:1661626-1664693		
J	27	200242	N/A	-0.5646	0.8669	Gtr1/RagA G protein	scaffold_5:1713676-1714749		
J	27	180771	N/A	-0.7979	1.2288	-	scaffold_5:1832881-1836817		
J	27	180710	N/A	-0.8181	1.1747	-	scaffold_5:2117034-2117949		
J	27	209231	N/A	-0.6001	0.8285	Aldo/keto reductase	scaffold_5:32055-33111		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	27	181472	N/A	-0.695	1.2262	ER lumen protein retaining receptor	scaffold_5:809818-810867		
J	27	181577	N/A	-0.7151	1.0137	hypothetical protein with predicted ABC, SMC and ATP/GTP -binding site motif A; KOG Class: Chromatin structure and dynamics; KOG Id: 0996; KOG description: Structural maintenance of chromosome protein 4 (chromosome condensation complex Condensin, subunit C)	scaffold_5:932052-936519		
J	27	210265	N/A	-0.4816	0.8382	Molybdenum cofactor biosynthesis protein	scaffold_6:1444165-1446474		
J	27	48817	N/A	-0.6937	1.1364	Transcription initiation factor IIA, gamma subunit	scaffold_6:1494218-1494698	104	
J	27	128349	N/A	-0.7149	1.3425	-	scaffold_6:1495101-1495310	104	
J	27	182322	N/A	-0.6377	0.9569	Gamma-tubulin ring complex protein	scaffold_6:1510943-1513336		
J	27	182560	N/A	-0.7386	1.1305	Importin-beta, N-terminal	scaffold_6:1546463-1549691		
J	27	137591	N/A	-0.5221	0.7196	-	scaffold_6:439332-439838		
J	27	53410	N/A	-0.7662	1.1198	-	scaffold_6:464991-467484		
J	27	200428	N/A	-0.5303	0.6792	WD40 repeat-containing protein	scaffold_6:56407-58775		
J	27	127000	N/A	-0.7256	1.0515	-	scaffold_7:253022-253846		
J	27	210458	N/A	-0.8052	1.2605	Predicted protein shares amino acid sequence identiy with the Saccharomyces cerevisiae SKI2 gene product; a putative RNA helicase, involved in exosome mediated 3' to 5' mRNA degradation and translation inhibition of non-poly(A) mRNAs; forms complex with Ski3p and Ski8p; required for repressing propagation of dsRNA viruses.	scaffold_7:318600-322740		
J	27	53582	N/A	-0.4784	0.8208	-	scaffold_7:399082-400352	105	
J	27	183811	N/A	-0.4359	0.8094	-	scaffold_7:403515-404516	105	
J	27	41067	N/A	-0.4524	0.7585	Predicted tubulin-tyrosine ligase	scaffold_7:539480-542111		
J	27	41125	N/A	-0.4158	0.6169	-	scaffold_7:724749-727862		
J	27	53646	N/A	-0.627	0.8948	-	scaffold_7:829557-830129		
J	27	185299	N/A	-0.9142	1.2472	Glycosyl transferase, group 1	scaffold_8:1404067-1405578		
J	27	49216	N/A	-0.5678	0.9276	Alpha/gamma adaptin	scaffold_8:152437-155423		
J	27	201380	N/A	-0.3863	0.6643	peptidyl-prolyl cis-trans isomerase	scaffold_8:240446-241189		
J	27	56504	N/A	-0.8316	1.184	Hypothetical protein with RCC1 domain	scaffold_8:26617-28397		
J	27	56536	N/A	-0.527	0.767	-	scaffold_8:287148-288013		
J	27	185679	N/A	-0.7906	1.2592	Tyrosine specific protein phosphatase	scaffold_8:38381-40183		
J	27	53717	N/A	-0.7049	1.0526	AAA ATPase	scaffold_8:52512-53844		
J	27	202059	N/A	-0.5148	1.0375	Isochorismatase hydrolase	scaffold_9:1126072-1126905		
J	27	42464	N/A	-0.6086	1.1328	candidate Peptidyl-prolyl cis-trans isomerase	scaffold_9:1309134-1309859		
J	27	202139	N/A	-0.6855	0.9035	Ubiquitin-like protein	scaffold_9:1422630-1423224	106	
J	27	186371	N/A	-0.7667	1.0955	-	scaffold_9:1423776-1424873	106	
J	27	42545	N/A	-0.7301	1.1085	-	scaffold_9:1611272-1613005		
J	27	186696	N/A	-0.618	0.8981	Peptidase M	scaffold_9:1628516-1629374	107	
J	27	42553	N/A	-0.771	1.1248	-	scaffold_9:1631422-1632355	107	
J	27	202202	N/A	-0.7351	1.0596	Hypothetical. Ca2+-binding actin-bundling protein (fimbrin/plastin)	scaffold_9:1664390-1666625		
J	27	202206	N/A	-0.5815	0.8068	Gamma-glutamyl phosphate reductase	scaffold_9:1673898-1675370		
J	27	186700	N/A	-0.5535	0.9266	-	scaffold_9:520413-522355	108	
J	27	185993	N/A	-0.7322	1.1606	Ubiquitin-like protein	scaffold_9:523184-523396	108	
J	27	211509	N/A	-0.5055	0.6585	Fungal specific transcription factor	scaffold_9:675612-677735		
J	27	185698	N/A	-0.5606	1.0096	-	scaffold_9:898757-899646		
J	28	35701	N/A	-0.7404	1.0624	-	scaffold_1:1088129-1089302		
J	28	51857	N/A	-0.715	1.2395	-	scaffold_1:1641309-1641932		
J	28	205979	N/A	-0.8368	0.976	Serine/threonine protein kinase	scaffold_1:2200049-2202459		
J	28	170355	N/A	-1.2193	1.5667	-	scaffold_1:2958126-2960693		
J	28	52017	N/A	-0.3852	0.687	-	scaffold_1:3083053-3083730		
J	28	170223	N/A	-0.6065	0.9922	putative GH family 81 endo-1,3-beta-glucanase	scaffold_1:3098148-3101339		
J	28	35486	N/A	-0.6126	0.6506	-	scaffold_1:380073-381437		
J	28	170198	N/A	-0.8545	0.9658	SAM (and some other nucleotide) binding motif	scaffold_1:616621-617890		
J	28	120259	N/A	-0.5489	0.9652	Glycosyl transferase, family 8	scaffold_10:1058862-1061314		
J	28	54207	N/A	-0.435	0.7546	MaoC-like dehydratase	scaffold_10:1212263-1213530		
J	28	212140	N/A	-0.6431	1.0073	hypothetical cAMP-dependent protein kinase catalytic subunit	scaffold_10:1240493-1243262		
J	28	43044	N/A	-0.5942	0.6964	Hypothetical protein. Is very likely associated with degradation of aromatic compounds based on Pfam and protein similarity	scaffold_10:1962829-1963824		
J	28	188006	N/A	-0.4882	0.6841	Phospholipid/glycerol acyltransferase	scaffold_10:391005-393571		
J	28	202289	N/A	-0.5582	0.8822	-	scaffold_10:404044-405264		
J	28	43391	N/A	-0.7551	1.425	Dehydrogenase E1 component	scaffold_11:1116999-1118555		
J	28	50197	N/A	-1.1371	1.6561	Hypothetical protein. PFam suggests a Enoyl-CoA hydratase/isomerase function	scaffold_11:1247318-1248297		
J	28	212416	N/A	-0.6441	0.9572	-	scaffold_11:283137-284366		
J	28	54281	N/A	-0.9129	1.2148	O-acetylhomoserine/O-acetylserine sulfhydrylase (cysD) EC 2.5.1.47	scaffold_11:62938-64580		
J	28	50131	N/A	-0.5888	1.1861	hypothetical Pyridoxal-5'-phosphate-dependent enzyme, β subunit	scaffold_11:800291-801497		
J	28	188804	N/A	-0.5221	0.5839	-	scaffold_11:988212-988475		
J	28	50306	N/A	-0.3762	0.4684	hypothetical ThiamineS, sulfur metabolism	scaffold_12:328935-329201		
J	28	212884	N/A	-0.4755	0.67	-	scaffold_12:421187-422314	109	
J	28	189912	N/A	-0.4446	0.8205	-	scaffold_12:423494-424585	109	
J	28	212783	N/A	-0.5095	0.894	putative GH family 47 mannosyl-oligosaccharide 1,2-alpha-mannosidase	scaffold_12:87863-91108		
J	28	44318	N/A	-0.3991	0.7932	-	scaffold_13:1073898-1075037		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	28	190566	N/A	-0.3039	0.3771	Predicted endoplasmic reticulum membrane protein Lec35	scaffold_13:417389-418341		
J	28	203665	N/A	-0.5551	0.7844	emp24/gp25L/p24 family of membrane trafficking proteins	scaffold_13:741564-742403		
J	28	191332	N/A	-0.4804	0.6972	Serine/threonine kinase receptor-associated protein	scaffold_14:348091-349369		
J	28	54678	N/A	-1.1335	1.6935	Hypothetical heterokaryon incompatibility factor	scaffold_14:39611-41435		
J	28	44492	N/A	-0.9973	1.3711	ABC transporter	scaffold_14:461452-465372		
J	28	191206	N/A	-0.5807	1.1693	Aminoacyl-tRNA synthetase	scaffold_14:818760-820038		
J	28	191330	N/A	-0.4559	0.829	-	scaffold_14:925744-926816	110	
J	28	50782	N/A	-0.5627	0.7214	Cytidine deaminase, homotetrameric	scaffold_14:930822-931636	110	
J	28	54785	N/A	-0.796	1.1605	-	scaffold_15:156651-158553		
J	28	192222	N/A	-0.8862	0.9316	hypothetical amine oxidase	scaffold_15:619393-621235		
J	28	45282	N/A	-1.0582	1.461	-	scaffold_17:108964-109895		
J	28	133160	N/A	-0.7053	0.955	Beta subunit of farnesyltransferase	scaffold_17:245782-247541		
J	28	133835	N/A	-0.2616	0.3522	Aminotransferase	scaffold_17:523503-525218		
J	28	193197	N/A	-0.4501	0.5191	Splicing coactivator SRm160/300, subunit SRm300	scaffold_17:675898-678641		
J	28	45507	N/A	-0.5072	0.6826	Protein OS-9	scaffold_18:219336-221074		
J	28	51325	N/A	-0.5719	1.1457	Aldehyde dehydrogenase	scaffold_18:528408-530040		
J	28	52238	N/A	-0.3773	0.6787	Hypothetical Aromatic aminotransferase, expression is regulated by general control of amino acid biosynthesis, EC 2.6.1.57	scaffold_2:1399674-1401634		
J	28	197539	N/A	-0.3021	0.5144	Transcription factor of the Forkhead/HNF3 family	scaffold_2:1998634-2000912		
J	28	175174	N/A	-0.6316	1.0195	Ctr copper transporter family	scaffold_2:3257749-3258661		
J	28	124393	N/A	-0.4735	0.6528	Peroxisomal NUDIX hydrolase	scaffold_2:3274661-3275931		
J	28	174884	N/A	-0.6129	1.0487	Hypothetical Cytochrome P450 monooxygenase	scaffold_2:3772823-3774760		
J	28	173771	N/A	-0.9503	1.267	Major facilitator superfamily	scaffold_2:3977449-3979352		
J	28	207539	N/A	-0.7387	1.2243	UBA/THIF-type NAD/FAD binding fold	scaffold_2:4001841-4004194		
J	28	206472	N/A	-0.4882	0.7598	Translocation protein Sec62	scaffold_2:404455-405586		
J	28	206569	N/A	-0.2927	0.5151	Hypothetical DNA polymerase α, catalytic subunit	scaffold_2:655542-662413		
J	28	206586	N/A	-0.4076	0.7814	Vacuolar assembly/sorting protein	scaffold_2:715586-717844		
J	28	174157	N/A	-0.7918	1.5467	Hypothetical alcohol dehydrogenase; EC 1.1.1.1	scaffold_2:747760-749263		
J	28	174927	N/A	-0.6461	0.9247	-	scaffold_2:770184-772135		
J	28	128697	N/A	-0.336	0.5594	AAA ATPase	scaffold_20:50346-56979		
J	28	55781	N/A	-0.5121	0.8939	-	scaffold_3:2112120-2115314		
J	28	125535	N/A	-0.3813	0.5184	Acyl-coA-binding protein, ACBP	scaffold_3:2261439-2262744		
J	28	52706	N/A	-0.7903	0.9806	Nucleoside phosphatase	scaffold_3:2372537-2374335		
J	28	177822	N/A	-0.5885	0.9124	Thioredoxin-like protein	scaffold_3:3451808-3452715		
J	28	175695	N/A	-0.2882	0.3731	-	scaffold_3:3465395-3465844		
J	28	119729	N/A	-0.6505	0.833	Cation efflux protein	scaffold_3:495442-498253		
J	28	52540	N/A	-0.7833	1.1595	related to UV-endonuclease Uve1p/UVDE	scaffold_3:534261-535966		
J	28	207636	N/A	-0.4675	0.8397	hypothetical non-ribosomal peptide synthetase	scaffold_3:544139-558370		
J	28	179558	N/A	-0.5926	0.9577	-	scaffold_4:1609968-1611011		
J	28	39194	N/A	-0.7043	1.1143	Hypothetical protein kinase	scaffold_4:1697363-1698817		
J	28	178266	N/A	-0.6132	0.8476	Major facilitator superfamily	scaffold_4:1757229-1758933		
J	28	141132	N/A	-0.7908	1.0197	Deduced amino acid sequence shares identity with mitochondrial polypeptide chain release factor, involved in stop codon recognition and hydrolysis of the peptidyl-tRNA bond during mitochondrial translation. lack of MRF1 causes mitochondrial genome instability in Saccharomyces cerevisiae.	scaffold_4:2912245-2913451		
J	28	52938	N/A	-0.4997	1.0076	Esterase/lipase/thioesterase	scaffold_4:917495-918468		
J	28	181089	N/A	-0.5524	0.7581	Hypothetical peroxisomal NUDIX hydrolase	scaffold_5:133317-134701		
J	28	209754	N/A	-0.8133	1.1963	2-nitropropane dioxygenase	scaffold_5:1692742-1693897		
J	28	180613	N/A	-0.9175	1.2078	Hypothetical guanine nucleotide exchange factor	scaffold_5:1967584-1973767		
J	28	139753	N/A	-0.8006	1.1026	-	scaffold_5:427592-429677		
J	28	209506	N/A	-0.5489	0.789	hypothetical alkaline phosphatase	scaffold_5:752748-754591		
J	28	130735	N/A	-0.8739	1.1281	-	scaffold_5:842793-844950		
J	28	39592	N/A	-0.6887	1.0238	Polyadenylate-binding protein (RRM superfamily)	scaffold_5:94156-94703		
J	28	56350	N/A	-0.6748	0.9428	-	scaffold_6:1479595-1480891		
J	28	40785	N/A	-0.7069	0.8855	-	scaffold_6:1639217-1641404		
J	28	48646	N/A	-0.5389	0.8737	Hypothetical enoyl-CoA hydratase (EC 4.2.1.17)	scaffold_6:462234-463132		
J	28	210080	N/A	-1.0437	1.4386	Signal recognition particle	scaffold_6:563285-565337		
J	28	49092	N/A	-0.6453	0.998	Predicted membrane proteins, contain hemolysin III domain	scaffold_7:1268079-1270269		
J	28	210760	N/A	-0.6693	0.9528	-	scaffold_7:1465537-1468260		
J	28	184314	N/A	-0.4354	0.5952	-	scaffold_7:387753-389563		
J	28	200992	N/A	-0.9055	1.235	-	scaffold_7:422229-423062		
J	28	125644	N/A	-0.5389	0.8457	Short-chain dehydrogenase/reductase SDR	scaffold_7:430233-431413		
J	28	40922	N/A	-0.4294	0.7362	Predicted dehydrogenase	scaffold_7:85751-86488		
J	28	185646	N/A	-0.6447	1.1502	6-phosphogluconate dehydrogenase, NAD-binding	scaffold_8:1089762-1091165		
J	28	210871	N/A	-0.8909	1.1644	3-hydroxyacyl-CoA dehydrogenase	scaffold_8:115896-116998		
J	28	56607	N/A	-0.6203	0.8145	Armadillo/beta-catenin-like repeats	scaffold_8:1218423-1220470		
J	28	211267	N/A	-0.6508	0.9252	Kinesin, motor region	scaffold_8:1478559-1480680		
J	28	41637	N/A	-0.6161	0.9452	Calcium-binding EF-hand	scaffold_8:559885-560350		
J	28	211076	N/A	-1.4053	2.476	-	scaffold_8:798642-800028		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	28	186422	N/A	-0.8891	1.5109	Sterol O-acyltransferase/Diacylglycerol O-acyltransferase	scaffold_9:1366753-1368358		
J	28	211749	N/A	-0.9762	1.2686	Mitochondrial solute carrier protein	scaffold_9:1677251-1678550		
J	28	186407	N/A	-0.7634	1.0914	Thioesterase superfamily	scaffold_9:309498-310380		
J	28	211346	N/A	-0.9105	1.39	-	scaffold_9:4963-6111		
J	29	172485	N/A	-0.7341	0.8582	Predicted membrane protein	scaffold_1:1003215-1005066		
J	29	51829	N/A	-0.222	0.364	Clathrin-associated protein medium chain	scaffold_1:1420449-1422495		
J	29	35412	N/A	-0.5984	0.7517	FAD linked oxidase, N-terminal	scaffold_1:146081-147631		
J	29	35842	N/A	-0.4483	0.7384	-	scaffold_1:1526200-1528571		
J	29	51890	N/A	-0.5319	0.7217	Candidate CotA	scaffold_1:1919422-1921545		
J	29	51892	N/A	-0.5695	0.6547	Fungal specific transcription factor	scaffold_1:1929141-1931435		
J	29	170172	N/A	-0.4227	0.6117	similar to α-L-rhamnosidase rhaA of Aspergillus aculeatus	scaffold_1:2059645-2061661		
J	29	171346	N/A	-0.9712	1.331	-	scaffold_1:2103105-2104817		
J	29	46625	N/A	-0.9108	1.1414	-	scaffold_1:2203679-2205802		
J	29	205986	N/A	-0.6547	1.3939	-	scaffold_1:2222318-2223144		
J	29	55417	N/A	-1.3027	1.781	Serine/threonine protein kinase, active site	scaffold_1:2425679-2426953		
J	29	55237	N/A	-0.4826	0.6164	-	scaffold_1:273479-274333		
J	29	36238	N/A	-0.3991	0.6089	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 4191; KOG Description: Histone acetyltransferases PCAF/SAGA/ADA, subunit TADA3L/NGG1	scaffold_1:2989082-2991227		
J	29	137631	N/A	-0.4565	0.6728	-	scaffold_1:3337589-3338146		
J	29	55241	N/A	-0.4687	0.7662	Fungal specific transcription factor	scaffold_1:360854-364586		
J	29	51718	N/A	-0.3377	0.6905	hypothetical protein with Zn-finger domain	scaffold_1:375191-376294		
J	29	35379	N/A	-0.6921	0.9599	Major facilitator superfamily	scaffold_1:50051-51689		
J	29	172633	N/A	-0.511	0.728	-	scaffold_1:881484-882669		
J	29	134049	N/A	-0.3436	0.398	UDP-galactose transporter related protein	scaffold_10:1016832-1018181		
J	29	187701	N/A	-0.5049	0.6563	Electron transporter activity	scaffold_10:1689977-1690885		
J	29	54233	N/A	-0.6334	0.9315	Glycosyl transferases group 1	scaffold_10:1781732-1783477		
J	29	188089	N/A	-0.3394	0.6162	hypothetical protein with galactose oxidase and transmembrane domains	scaffold_10:1806430-1809243		
J	29	56841	N/A	-0.3215	0.6982	putative transmembrane GH family 47 mannosyl-oligosaccharide 1,2-alpha-mannosidase	scaffold_10:1870617-1872934		
J	29	212272	N/A	-0.8664	1.1462	Hypothetical G-protein with WD-40 repeat	scaffold_10:1949997-1951276		
J	29	212285	N/A	-0.6556	0.7847	Protein of unknown function (DUF396)	scaffold_10:1977734-1978578		
J	29	43508	N/A	-0.4967	0.6735	-	scaffold_11:1455480-1456972		
J	29	212363	N/A	-0.4231	0.5664	Protein kinase	scaffold_11:153142-154277	111	
J	29	188287	N/A	-0.8875	1.2577	Hypothetical silent information regulator protein of the Sir2 family	scaffold_11:154826-155980	111	
J	29	212395	N/A	-0.5706	0.6808	Peptidase M18, aminopeptidase I	scaffold_11:225222-228612		
J	29	56895	N/A	-0.7877	0.8739	Thymidylate kinase/adenylate kinase	scaffold_11:315365-316101		
J	29	212337	N/A	-1.0247	1.079	Hypothetical protein. Contains four putative transmembrane helices	scaffold_11:60484-61135		
J	29	43345	N/A	-0.4251	0.7043	Amino acid transporter	scaffold_11:960935-962698		
J	29	190025	N/A	-0.6912	0.9247	Major facilitator superfamily	scaffold_12:1144670-1145997		
J	29	54468	N/A	-0.7046	1.3092	Amidases	scaffold_12:291430-293383		
J	29	190396	N/A	-0.3338	0.6515	-	scaffold_13:1024192-1025436		
J	29	54649	N/A	-0.9583	1.2067	Hypothetical dehydroquinase	scaffold_13:1038443-1040536		
J	29	203471	N/A	-0.7484	1.0043	Thioredoxin-like protein	scaffold_13:180415-181620		
J	29	191021	N/A	-0.4769	0.6441	-	scaffold_13:318385-319438		
J	29	57028	N/A	-0.5371	0.6801	Aldehyde dehydrogenase	scaffold_13:345617-347236		
J	29	131243	N/A	-0.5619	0.9095	Flavoprotein monooxygenase	scaffold_13:35758-37640		
J	29	54556	N/A	-0.3397	0.5886	-	scaffold_13:358674-360222		
J	29	190726	N/A	-0.7011	0.7956	-	scaffold_13:704818-706245		
J	29	134018	N/A	-0.579	0.686	-	scaffold_13:935875-937152		
J	29	203924	N/A	-0.4219	0.5837	putative protein transport protein SEC61 subunit α. Probable endoplasmic reticulum	scaffold_14:297116-298828		
J	29	213492	N/A	-0.7759	1.0902	Glycosyltransferase, family 2	scaffold_14:313839-315299		
J	29	44373	N/A	-0.8277	1.5572	Mitochondrial carnitine-acylcarnitine carrier protein	scaffold_14:55414-56611		
J	29	57172	N/A	-1.0934	1.4534	-	scaffold_14:855773-856707		
J	29	44666	N/A	-0.9621	1.4897	-	scaffold_15:45879-46718		
J	29	193012	N/A	-0.7171	0.9167	Ubiquitin-protein ligase	scaffold_16:113322-113893		
J	29	213947	N/A	-0.3538	0.4575	Hypothetical protein with RRM domain	scaffold_16:395069-396540		
J	29	204737	N/A	-0.7462	0.7869	-	scaffold_17:387198-388440		
J	29	45374	N/A	-0.6462	0.8061	ATP/GTP-binding site motif A	scaffold_17:434304-435391		
J	29	128453	N/A	-0.6191	0.7375	-	scaffold_17:454015-454514	112	5
J	29	55007	N/A	-0.7228	1.1935	related to 3-ketoacyl-CoA thiolase	scaffold_17:457596-458976	112	5
J	29	55008	N/A	-1.0325	1.1869	Hypothetical HSP90 co-chaperone CPR7/Cyclophilin	scaffold_17:461190-463860	112	5
J	29	45263	N/A	-0.2744	0.3462	-	scaffold_17:62206-62789		
J	29	193777	N/A	-0.8944	1.3281	DEAD/DEAH box helicase	scaffold_18:285677-301535	113	
J	29	193909	N/A	-0.4503	0.6599	Ureidoglycolate hydrolase	scaffold_18:305258-306022	113	
J	29	121949	N/A	-1.1418	1.3326	-	scaffold_18:40377-42003		
J	29	45623	N/A	-0.7997	0.9627	-	scaffold_18:621080-622289		
J	29	214458	N/A	-0.861	1.2903	-	scaffold_18:78446-80152	114	
J	29	214460	N/A	-0.734	0.9732	Serine carboxypeptidase	scaffold_18:80628-82815	114	
J	29	206723	N/A	-0.7197	1.199	-	scaffold_2:1113951-1116636		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	29	173038	N/A	-0.5685	0.6257	WD40 repeat protein	scaffold_2:1156716-1159940		
J	29	52241	N/A	-0.7004	0.8601	Glyoxalase	scaffold_2:1428711-1429337		
J	29	52248	N/A	-0.963	1.1928	Protein kinase	scaffold_2:1469443-1471574		
J	29	197381	N/A	-0.6228	0.821	GTPase Rab5/YPT51 and related small G protein superfamily GTPases	scaffold_2:1588269-1589319		
J	29	197415	N/A	-0.9479	1.3292	putative extracellular proteins sharing 38% amino acid sequence identity with Aspergillus oryzae glutaminase A (PMID: 10952006)	scaffold_2:1681745-1684484		
J	29	52334	N/A	-0.6697	0.8345	-	scaffold_2:2415120-2417984		
J	29	174463	N/A	-0.7708	0.9212	Hypothetical protein with TPR repeat	scaffold_2:2903099-2905419		
J	29	197766	N/A	-0.5164	0.7698	-	scaffold_2:3137098-3138781		
J	29	129181	N/A	-0.397	0.57	-	scaffold_2:326595-329296		
J	29	197881	N/A	-0.5911	0.7052	Mov34 family	scaffold_2:3420437-3422137		
J	29	173081	N/A	-0.5018	0.7148	Hypothetical protein. Transport activity is a probable function due to 12 predicted transmembrane domains.	scaffold_2:3622699-3624485		
J	29	37539	N/A	-0.8215	1.2547	Related to norsolorinic acid reductase from Aspergillus fumigatus and Aspergillus flavus where it is part of the aflatoxin cluster	scaffold_2:3650477-3651871		
J	29	47182	N/A	-0.619	0.6967	-	scaffold_2:3829187-3829777		
J	29	122575	N/A	-0.7688	1.0013	-	scaffold_2:584104-585686		
J	29	173300	N/A	-0.4393	0.6504	-	scaffold_2:877270-879158		
J	29	51449	N/A	-1.2516	1.4454	Hypothetical. Monocarboxylate transporter. Signal P suggests secretion	scaffold_20:287403-288788		
J	29	55156	N/A	-0.6654	1.0511	FOG: Zn-finger	scaffold_20:42204-45809		
J	29	51406	N/A	-0.4624	0.467	-	scaffold_20:85561-86461		
J	29	55193	N/A	-0.9353	1.135	-	scaffold_21:239611-240677		
J	29	207885	N/A	-0.899	1.0702	Cdc4 and related F-box and WD-40 proteins	scaffold_3:1702861-1706282		
J	29	47464	N/A	-0.7845	0.985	Protein of unknown function DUF6	scaffold_3:1924738-1926093		
J	29	198494	N/A	-0.872	1.2013	-	scaffold_3:1988195-1989149		
J	29	208069	N/A	-0.5718	0.7993	-	scaffold_3:2163427-2165012		
J	29	198577	N/A	-1.0827	1.2076	Carnitine O-acyltransferase	scaffold_3:2245800-2248399		
J	29	38375	N/A	-0.6432	0.8989	Major facilitator superfamily	scaffold_3:2631703-2633465		
J	29	208179	N/A	-0.3482	0.7382	Surf 4 protein. ER to Golgi transport	scaffold_3:2650979-2652249		
J	29	208244	N/A	-0.7395	0.9775	Protein kinase	scaffold_3:2821557-2824896		
J	29	52756	N/A	-0.7594	0.8843	-	scaffold_3:2844317-2847429		
J	29	176865	N/A	-0.3639	0.6299	Hypothetical GPI anchor protein	scaffold_3:2989299-2990541		
J	29	47696	N/A	-0.7462	1.3039	-	scaffold_3:3266850-3267689		
J	29	176250	N/A	-0.4893	0.7368	Glycoside hydrolase, family 1	scaffold_3:3446363-3446916		
J	29	176010	N/A	-0.7681	0.9654	Predicted esterase of the α-β hydrolase superfamily	scaffold_3:3479771-3481756		
J	29	208484	N/A	-0.3974	0.8053	Signal transduction	scaffold_3:3521993-3522633		
J	29	38678	N/A	-0.3548	0.4121	-	scaffold_3:3594509-3594870		
J	29	135400	N/A	-0.8797	1.1445	-	scaffold_3:403888-404874		
J	29	47266	N/A	-0.6241	0.664	Nonaspanin	scaffold_3:523523-525621		
J	29	52545	N/A	-0.5464	0.6628	RNA recognition motif. (a.k.a. RRM, RBD, or RNP domain)	scaffold_3:596272-598307		
J	29	126298	N/A	-0.582	0.7508	Mitochondrial carrier protein	scaffold_3:775186-776173		
J	29	207747	N/A	-0.5382	0.8045	-	scaffold_3:855401-861924		
J	29	48030	N/A	-0.3653	0.5906	Hypothetical Gpi16 subunit, GPI transamidase component	scaffold_4:1740381-1742274		
J	29	208544	N/A	-0.3509	0.6316	Candidate ribose 5-phosphate isomerase	scaffold_4:179761-180659		
J	29	53082	N/A	-0.4273	0.707	Related to histone 1 protein, H1, with a predicted H1/H5 domain, histone linker N- terminal, and winged helix DNA binding. The protein is essential for chromatin stucture and links nucleosomes in higher order structures; KOG Class: Chromatin structure and dynamics; KOG Id: 4012; KOG Description: Histone H1	scaffold_4:2673351-2674637		
J	29	199618	N/A	-0.6103	0.999	-	scaffold_4:2712045-2713023		
J	29	53116	N/A	-0.8475	1.2876	-	scaffold_4:2931870-2933553		
J	29	47819	N/A	-0.6279	1.0923	-	scaffold_4:339344-340489	115	
J	29	38782	N/A	-0.9977	1.5172	Serine/threonine protein kinase	scaffold_4:340686-342129	115	
J	29	39893	N/A	-0.8784	1.6178	Synaptic vesicle transporter SVOP	scaffold_5:1129977-1131933		
J	29	180706	N/A	-0.6325	0.8979	hypothetical protein with a predicted histone-fold; GO Desc: DNA binding; GO Id: 3677; Interpro Desc: Histone-fold/TFIID-TAF/NF-Y	scaffold_5:132433-132900		
J	29	209366	N/A	-0.8546	1.1732	-	scaffold_5:353339-353881		
J	29	181216	N/A	-1.1607	1.5519	Kinesin light chain	scaffold_5:388811-390817		
J	29	48217	N/A	-0.6284	0.9669	Hypothetical peroxisomal biogenesis protein	scaffold_5:43646-45007		
J	29	210268	N/A	-0.7641	0.9001	Hypothetical Vacuolar H+-transporting two-sector ATPase	scaffold_6:1446940-1447789		
J	29	53405	N/A	-0.6001	0.9159	-	scaffold_6:399936-401363		
J	29	209940	N/A	-1.1094	1.3892	-	scaffold_6:40410-40851		
J	29	41311	N/A	-0.8449	1.102	Insulinase-like	scaffold_7:1381863-1385506		
J	29	53687	N/A	-0.5484	1.0007	Glutathione S-transferase	scaffold_7:1435247-1435900		
J	29	56431	N/A	-0.5396	0.9457	hypothetical galactokinase	scaffold_7:510980-512674		
J	29	133565	N/A	-0.6628	1.2336	-	scaffold_7:549108-549848		
J	29	183596	N/A	-0.6998	0.9491	Integral membrane protein involved in transport between the late Golgi and endosome	scaffold_7:707216-707944		
J	29	56519	N/A	-0.862	1.1618	-	scaffold_8:102343-103782		
J	29	211114	N/A	-0.7088	1.0384	-	scaffold_8:942462-943532		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	29	186514	N/A	-0.96	1.1881	Chitinase	scaffold_9:1127043-1128786		
J	29	42470	N/A	-0.5385	0.8127	-	scaffold_9:1320011-1324310		
J	29	211653	N/A	-0.3605	0.5022	-	scaffold_9:1360670-1362890		
J	29	42169	N/A	-0.7944	1.186	-	scaffold_9:451632-452480		
J	29	42171	N/A	-0.821	1.1625	Hypothetical isocitrate lyase and phosphorylmutase	scaffold_9:459486-461546		
J	29	120032	N/A	-0.6141	0.7809	Extracellular protein SEL-1 and related proteins	scaffold_9:484233-486616		
J	29	138063	N/A	-0.6939	1.103	-	scaffold_9:751599-751973		
J	30	172548	N/A	-0.7587	1.0151	-	scaffold_1:1318507-1320030		
J	30	129139	N/A	-0.8568	0.9572	Hypothetical actin regulatory protein	scaffold_1:1604192-1608081		
J	30	51871	N/A	-0.6963	0.8474	Fungal specific transcription factor	scaffold_1:1720323-1723049		
J	30	205927	N/A	-1.2137	1.4331	-	scaffold_1:2062330-2064501		
J	30	55412	N/A	-0.8003	1.0029	F-actin capping protein, β subunit	scaffold_1:2363255-2364371		
J	30	170231	N/A	-0.6006	0.7237	-	scaffold_1:3062709-3067387		
J	30	55469	N/A	-0.8357	1.0916	FAD dependent oxidoreductase	scaffold_1:3146077-3150059		
J	30	55487	N/A	-0.9568	1.2186	-	scaffold_1:3327728-3329708		
J	30	35478	N/A	-0.8414	0.9739	-	scaffold_1:358090-360126		
J	30	46294	N/A	-0.3194	0.4149	Related to PAP1, poly-A polymerase.	scaffold_1:382015-384097		
J	30	46358	N/A	-0.5423	0.9685	Hypothetical protein. May have catechol dioxygenase activity	scaffold_1:721845-722996		
J	30	54109	N/A	-0.8977	0.9778	Ras-related GTPase	scaffold_10:444392-445366		
J	30	42728	N/A	-0.6749	0.9752	related to vacuolar ATP synthase subunit D	scaffold_10:510042-511243		
J	30	211957	N/A	-0.7333	1.0187	protein phosphatase	scaffold_10:761415-763734		
J	30	54174	N/A	-0.824	1.0934	Dihydroxy-acid dehydratase	scaffold_10:985008-986961		
J	30	54330	N/A	-0.8741	1.0481	emp24/gp25L/p24 family of membrane trafficking proteins	scaffold_11:402471-403412		
J	30	43285	N/A	-0.6792	0.9011	Fungal transcriptional regulatory protein	scaffold_11:777671-779715		
J	30	212750	N/A	-0.8589	1.1242	FAD binding domain	scaffold_12:12003-14002		
J	30	43655	N/A	-1.3317	2.0772	Ank repeat	scaffold_12:248284-254113		
J	30	213396	N/A	-0.5779	0.7042	-	scaffold_13:1198382-1199081		
J	30	213045	N/A	-1.2886	1.5789	Lipid phosphate phosphatase and related enzymes of the PAP2 family	scaffold_13:230691-232252		
J	30	191038	N/A	-0.6482	0.8404	Amino acid/polyamine transporter	scaffold_13:624674-628424		
J	30	190324	N/A	-0.9426	1.2125	-	scaffold_13:675593-678279		
J	30	57079	N/A	-0.648	0.7746	Hypothetical DnaJ domain protein	scaffold_13:758123-759315		
J	30	212988	N/A	-0.8004	0.9954	-	scaffold_13:9427-10800		
J	30	128537	N/A	-1.0698	1.259	putative allergen	scaffold_13:949568-949885		
J	30	57134	N/A	-0.7854	0.9858	hypothetical protein; KOG Class: Chromatin structure and dynamics;	scaffold_14:164568-166334		
J	30	44367	N/A	-0.7322	0.9929	-	scaffold_14:34493-35578		
J	30	54758	N/A	-0.7346	0.8926	Predicted undecaprenyl diphosphate synthase	scaffold_14:944524-945710		
J	30	213733	N/A	-0.735	0.904	Predicted ubiquitin regulatory protein, contains UAS and UBX domains	scaffold_15:217418-219036		
J	30	191787	N/A	-0.5774	0.761	serine/threonine protein kinase	scaffold_15:27846-29195		
J	30	192623	N/A	-0.5132	0.7897	Hypothetical DNA helicase	scaffold_16:118447-120852		
J	30	192954	N/A	-0.9292	1.2497	Hypothetical peroxisomal assembly protein PEX3	scaffold_16:659497-661294		
J	30	54937	N/A	-0.5781	0.8167	Hypothetical prephenate hydratase	scaffold_16:868306-869307		
J	30	45304	N/A	-1.0614	1.2199	related to α-amylase; glycoside hydrolase, family 13	scaffold_17:182673-184545		
J	30	126807	N/A	-0.6769	0.7676	Preprotein translocase subunit	scaffold_18:126287-127202		
J	30	45500	N/A	-0.6834	0.9322	G-like protein containing WD-40 repeat	scaffold_18:202207-204386		
J	30	206767	N/A	-0.9173	0.9805	-	scaffold_2:1259962-1261125		
J	30	206779	N/A	-0.5126	0.5897	Core histone H2A/H2B/H3/H4	scaffold_2:1319231-1319787		
J	30	174131	N/A	-0.383	0.479	Protein kinase	scaffold_2:1394182-1396927		
J	30	174932	N/A	-0.5306	0.7528	-	scaffold_2:1515376-1519491		
J	30	175089	N/A	-0.5318	0.6976	NAD dependent epimerase	scaffold_2:2534216-2535169		
J	30	52387	N/A	-0.5535	0.7539	Hypothetical H+-transporting two-sector ATPase	scaffold_2:2976232-2978314		
J	30	207477	N/A	-1.0282	1.2392	-	scaffold_2:3826788-3828272		
J	30	207532	N/A	-0.7681	1.0342	-	scaffold_2:3990515-3991457		
J	30	206650	N/A	-0.5071	0.6481	Gamma-tubulin complex component	scaffold_2:889259-892096		
J	30	195145	N/A	-0.8323	1.073	-	scaffold_22:59158-59932		
J	30	175603	N/A	-0.7489	0.9216	von Willebrand factor and related coagulation proteins	scaffold_3:1191645-1194130		
J	30	38103	N/A	-0.7772	1.0451	Hypothetical Damage-specific DNA binding protein	scaffold_3:1577684-1581393		
J	30	47417	N/A	-1.2494	1.5901	Short-chain dehydrogenase/reductase	scaffold_3:1649034-1650187		
J	30	177953	N/A	-0.6945	0.9033	Hypothetical Zn finger protein with RING domain	scaffold_3:1756998-1762239		
J	30	208113	N/A	-0.7489	1.1366	Mitochondrial substrate carrier	scaffold_3:2365151-2368007		
J	30	208123	N/A	-0.5684	0.6734	Eukaryotic translation initiation factor	scaffold_3:2376400-2377220		
J	30	176542	N/A	-1.1713	1.3573	Related to chitin synthase chaperone-like protein	scaffold_3:2391818-2392979		
J	30	198730	N/A	-0.9681	1.2968	Cell membrane glycoprotein	scaffold_3:2805658-2807043		
J	30	208272	N/A	-0.4241	0.5264	Ubiquitin-like protein	scaffold_3:2912227-2912629		
J	30	208385	N/A	-0.579	0.7861	Stomatin	scaffold_3:3244840-3246256		
J	30	52803	N/A	-0.3596	0.4823	Mitochondrial substrate carrier	scaffold_3:3300950-3302135		
J	30	128550	N/A	-0.8047	1.1795	-	scaffold_3:3420351-3420643		
J	30	208472	N/A	-1.0392	1.2495	Glutaredoxin and related proteins	scaffold_3:3484481-3484985		
J	30	47745	N/A	-0.6661	0.8322	-	scaffold_3:3491730-3495886		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	30	177169	N/A	-0.8354	1.1919	hypothetical extracellular gluconolactonase	scaffold_3:3514654-3516083		
J	30	177726	N/A	-1.3255	1.6213	-	scaffold_3:352803-354343		
J	30	175678	N/A	-0.7098	0.9288	-	scaffold_3:840991-843030		
J	30	179323	N/A	-0.5944	0.8413	Protein synthesis factor, GTP-binding	scaffold_4:1141068-1142437		
J	30	56002	N/A	-0.9556	1.1813	Lipid phosphate phosphatase and related enzymes of the PAP2 family	scaffold_4:1406910-1408037		
J	30	179884	N/A	-0.5317	0.7338	Protein kinase	scaffold_4:1572342-1573835		
J	30	52997	N/A	-0.955	1.2146	E3 ubiquitin protein ligase	scaffold_4:1707057-1712863		
J	30	179341	N/A	-0.8983	1.0719	Myb, DNA-binding	scaffold_4:2411680-2413579		
J	30	53259	N/A	-0.9032	1.0423	Hypothetical chitin synthase	scaffold_5:1189469-1193129		
J	30	209660	N/A	-0.7069	0.8508	SWI-SNF chromatin-remodeling complex protein	scaffold_5:1393078-1396919		
J	30	56243	N/A	-0.4741	0.6932	Electron transfer flavoprotein	scaffold_5:1851176-1852393		
J	30	39569	N/A	-0.9783	1.2286	GTPase/ATPase	scaffold_5:28460-30889		
J	30	209414	N/A	-0.9215	1.0322	Hypothetical small nuclear ribonucleoprotein (Sm protein)	scaffold_5:492783-493261		
J	30	209521	N/A	-1.2374	1.5182	-	scaffold_5:830443-832626		
J	30	209577	N/A	-0.8135	1.0945	-	scaffold_5:999029-1003678		
J	30	40721	N/A	-0.661	0.7938	Ras-related protein	scaffold_6:1448309-1449264		
J	30	53400	N/A	-0.6456	0.7934	Peptidase	scaffold_6:267089-268330	116	
J	30	48631	N/A	-0.5269	0.7826	-	scaffold_6:273173-274648	116	
J	30	40397	N/A	-0.3021	0.3577	-	scaffold_6:444027-444860		
J	30	182309	N/A	-0.9331	1.2236	Glycoside hydrolase, family 3	scaffold_6:613208-616447		
J	30	40505	N/A	-0.7222	0.7761	-	scaffold_6:756995-757893		
J	30	184331	N/A	-0.6429	0.8594	-	scaffold_7:1313203-1314453		
J	30	53675	N/A	-0.6931	0.9513	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae SKI3 gene product; a protein involved in exosome mediated 3′ to 5′ mRNA degradation and translation inhibition of non-poly(A) mRNAs; forms complex with Ski2p and Ski8p; required for repressing propagation of dsRNA viruses.	scaffold_7:1324236-1328602		
J	30	183336	N/A	-0.4416	0.5635	-	scaffold_7:1473058-1474164	117	
J	30	184226	N/A	-0.8821	1.0572	Cell-cycle nuclear protein, contains WD-40 repeats	scaffold_7:1475523-1478155	117	
J	30	53581	N/A	-0.6438	0.984	DNA-dependent protein kinase	scaffold_7:390149-397494		
J	30	56432	N/A	-0.6086	0.7887	-	scaffold_7:537818-539241		
J	30	41147	N/A	-0.794	1.113	MADS box transcription factor	scaffold_7:804999-806951		
J	30	41177	N/A	-0.8936	1.042	Predicted E3 ubiquitin ligase	scaffold_7:880554-881706		
J	30	121906	N/A	-0.8916	1.1107	Vacuolar sorting protein VPS36	scaffold_8:216620-218618		
J	30	185464	N/A	-0.871	1.151	DnaJ domain protein	scaffold_8:828278-829138		
J	30	49343	N/A	-0.4708	0.6282	Myosin class II heavy chain	scaffold_8:885194-887051		
J	30	42387	N/A	-0.6476	0.7809	-	scaffold_9:1079895-1080239		
J	30	42449	N/A	-0.4916	0.7522	-	scaffold_9:1256972-1258339		
J	30	211691	N/A	-0.5034	0.6808	Protein containing adaptin N-terminal region	scaffold_9:1500529-1508949		
J	30	185751	N/A	-0.6307	0.8108	hypothetical lysophospholipase	scaffold_9:429196-430244		
J	30	186350	N/A	-0.6313	0.7245	hypothetical carboxylesterase	scaffold_9:825300-826160		
J	31	172691	N/A	-0.487	0.5777	Serine/threonine protein kinase	scaffold_1:1210409-1212191		
J	31	196195	N/A	-0.4138	0.496	-	scaffold_1:1279653-1280124		
J	31	171254	N/A	-0.8354	0.9988	-	scaffold_1:1348490-1349920		
J	31	55334	N/A	-0.833	0.981	Predicted E3 ubiquitin ligase	scaffold_1:1505610-1506716		
J	31	46699	N/A	-0.7893	0.9004	Hypothetical late Golgi protein sorting complex, subunit	scaffold_1:2782691-2785415		
J	31	51725	N/A	-0.6974	0.7877	-	scaffold_1:428485-429662		
J	31	54208	N/A	-0.8868	1.0879	AAA ATPase	scaffold_10:1216264-1217808		
J	31	42962	N/A	-0.6726	0.7023	Adenine nucleotide translocator	scaffold_10:1694766-1696047		
J	31	54129	N/A	-0.4393	0.5305	Isoflavone reductase	scaffold_10:624339-625365		
J	31	54401	N/A	-0.7964	0.9401	-	scaffold_11:1239814-1241199		
J	31	43110	N/A	-0.757	0.8923	Putative growth response protein	scaffold_11:177510-179621		
J	31	188313	N/A	-0.2762	0.3211	-	scaffold_11:201565-203446	118	
J	31	212379	N/A	-0.5525	0.6982	putative transmembrane GH family 18 endo-chitinase	scaffold_11:207738-208691	118	
J	31	50044	N/A	-0.821	1.004	related to ubiquitin conjugating enzyme	scaffold_11:258067-258682		
J	31	203333	N/A	-0.7119	0.845	-	scaffold_12:425351-426669		
J	31	213364	N/A	-0.6703	0.7332	-	scaffold_13:1140136-1141305		
J	31	213093	N/A	-0.5953	0.6245	Proteasome/cyclosome, regulatory subunit	scaffold_13:378101-381834		
J	31	213703	N/A	-0.5922	0.6745	-	scaffold_15:171026-172897		
J	31	213757	N/A	-0.9325	1.0783	Gamma-glutamyltranspeptidase	scaffold_15:340322-344359		
J	31	127896	N/A	-0.741	0.8549	-	scaffold_16:707822-708238		
J	31	55011	N/A	-0.4591	0.548	51kDa subunit of NADH:ubiquinone reductase (complex I); NADH dehydrogenase [Aspergillus niger]	scaffold_17:479706-481375	119	
J	31	45389	N/A	-0.7916	1.0002	Deduced translation product shares limited amino acid sequence identity with the Saccharomyces cerevisiae NUP49 gene product; a subunit of the Nsp1p-Nup57p-Nup49p-Nic96p subcomplex of the nuclear pore complex (NPC), required for nuclear export of ribosomes.	scaffold_17:482970-489722	119	
J	31	214408	N/A	-0.8742	0.9408	Nucleic acid-binding OB-fold	scaffold_17:642956-644062		
J	31	55040	N/A	-0.4608	0.5512	Mg/Fe superoxide dismutase	scaffold_17:672124-672997		
J	31	193639	N/A	-0.5341	0.5761	-	scaffold_18:201356-201739		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	31	37330	N/A	-0.9723	1.2095	-	scaffold_2:2999152-3000214		
J	31	175181	N/A	-0.9447	1.2042	Phox-like	scaffold_2:366880-368994		
J	31	175222	N/A	-0.6436	0.7251	Cell cycle-associated protein	scaffold_2:956815-958432		
J	31	131561	N/A	-0.973	1.0195	-	scaffold_20:222244-223517		
J	31	38256	N/A	-0.6886	0.7851	Glycoside hydrolase, family 5	scaffold_3:2090935-2092387		
J	31	38261	N/A	-0.5755	0.7087	-	scaffold_3:2108754-2109599		
J	31	52691	N/A	-0.5744	0.6247	-	scaffold_3:2230945-2233070		
J	31	55865	N/A	-0.8322	1.0222	DEAD/DEAH box helicase	scaffold_3:3184821-3188610		
J	31	52797	N/A	-0.4759	0.6127	WD40 repeat protein	scaffold_3:3233131-3236943		
J	31	199481	N/A	-0.4333	0.472	ETC complex I subunit conserved region	scaffold_4:2392379-2393165		
J	31	137168	N/A	-0.5867	0.6736	Predicted eukaryotic translation initiation factor SUI1	scaffold_4:2592059-2594526		
J	31	47809	N/A	-0.4185	0.5039	Protein phosphatase 1, regulatory subunit, and related proteins	scaffold_4:272164-277804		
J	31	178797	N/A	-0.8019	0.8629	Peptidase C12, ubiquitin carboxyl-terminal hydrolase 1	scaffold_4:2883525-2884701		
J	31	52880	N/A	-0.6277	0.7681	Zn-finger (putative), N-recognin	scaffold_4:425865-432375		
J	31	208738	N/A	-0.6363	0.7662	Predicted membrane protein, contains two CBS domains	scaffold_4:896920-899297		
J	31	199703	N/A	-0.7139	0.826	Hypothetical mitochondrial substrate carrier	scaffold_5:12841-14257		
J	31	181619	N/A	-0.6347	0.6955	Transcription-coupled repair protein	scaffold_5:560286-563222		
J	31	56109	N/A	-0.3281	0.3926	Adenylate kinase	scaffold_5:71859-72865		
J	31	209252	N/A	-0.8646	0.9856	Autophagy related protein, involved in membrane trafficking	scaffold_5:85856-86406		
J	31	128772	N/A	-0.4636	0.6221	-	scaffold_6:1740962-1746752		
J	31	209947	N/A	-1.0157	1.1029	Mitochondrial carrier protein	scaffold_6:44162-45349		
J	31	181768	N/A	-0.8477	0.953	Short-chain dehydrogenase	scaffold_6:483389-484747		
J	31	48719	N/A	-1.023	1.1165	Short-chain dehydrogenase/reductase	scaffold_6:821933-823162		
J	31	183219	N/A	-0.9723	1.033	hypothetical MOZ/SAS-like protein; KOG Class: Chromatin structure and dynamics; KOG Id: 2747; KOG description: Histone acetyltransferase (MYST family)	scaffold_7:783816-784823		
J	31	211010	N/A	-0.6695	0.7667	Protein kinase	scaffold_8:576747-578457		
J	31	201534	N/A	-0.4183	0.4763	-	scaffold_8:760539-761875		
J	31	128507	N/A	-0.8298	0.8464	candidate mitochondrial ATP synthase epsilon chain	scaffold_9:1035646-1036001		
J	31	211628	N/A	-0.8476	1.0105	Hypothetical RING finger membrane protein	scaffold_9:1283821-1288711		
J	31	56673	N/A	-0.3128	0.3937	Hypothetical fumarate hydratase	scaffold_9:409635-411655		
J	32	35728	N/A	-0.2396	0.4588	Hypothetical glyceraldehyde 3-phosphate dehydrogenase; EC 1.2.1.12	scaffold_1:1178941-1180238		
J	32	55306	N/A	-0.4579	0.7945	Aminotransferase class-III	scaffold_1:1220971-1223145		
J	32	172668	N/A	-0.737	0.9895	Aldehyde dehydrogenase	scaffold_1:1361069-1361964		
J	32	51831	N/A	-0.3635	0.5632	-	scaffold_1:1456065-1458365		
J	32	125759	N/A	-0.7315	1.0526	Alkaline phytoceramidase	scaffold_1:1828176-1829326		
J	32	172145	N/A	-0.3997	0.5433	-	scaffold_1:1845431-1847025		
J	32	171484	N/A	-0.5269	0.738	Fungal transcriptional regulatory protein	scaffold_1:1953403-1956157		
J	32	172005	N/A	-0.3544	0.439	-	scaffold_1:2106707-2107794		
J	32	130152	N/A	-0.5836	0.8678	-	scaffold_1:2418054-2420498		
J	32	46678	N/A	-0.435	0.5849	Hypothetical adenylate kinase	scaffold_1:2506755-2507539		
J	32	170641	N/A	-0.6562	0.9037	Hypothetical protein with HECT domain	scaffold_1:2998558-3002263		
J	32	205426	N/A	-0.7855	0.8821	Peptidase	scaffold_1:390698-391906		
J	32	205450	N/A	-0.7157	0.9256	-	scaffold_1:464137-466369		
J	32	172390	N/A	-0.3214	0.5621	Manganese and iron superoxide dismutase	scaffold_1:646924-647678		
J	32	35560	N/A	-0.5777	0.9268	Aromatic amino acid aminotransferase and related proteins	scaffold_1:672343-673840		
J	32	171440	N/A	-0.3691	0.694	Fungal specific transcription factor	scaffold_1:690398-692845		
J	32	212055	N/A	-0.2445	0.2623	40S ribosomal protein S12	scaffold_10:1030445-1031070		
J	32	54223	N/A	-0.4764	0.554	Cytosolic sorting protein	scaffold_10:1738916-1741381		
J	32	49807	N/A	-0.4933	0.6954	Fungal transcriptional regulatory protein,	scaffold_10:362286-364620		
J	32	124139	N/A	-0.7184	1.0337	-	scaffold_10:441944-443475		
J	32	202315	N/A	-0.6974	0.837	-	scaffold_10:450291-453075		
J	32	56788	N/A	-0.6087	0.994	hypothetical protease that contains peptidase M28 domain	scaffold_10:932798-935207		
J	32	43463	N/A	-0.318	0.4057	-	scaffold_11:1344074-1344399		
J	32	56887	N/A	-0.4569	0.6931	hypothetical TAF6 subunit protein (Transcription initiation factor TFIID) with predicted histone-fold; KOG Class: Transcription; KOG Id: 2549; KOG description: Transcription initiation factor TFIID, subunit TAF6 (also component of histone acetyltransferase SAGA)	scaffold_11:264894-266360		
J	32	188319	N/A	-0.5444	0.6956	-	scaffold_11:278720-279227		
J	32	43225	N/A	-0.3763	0.4663	-	scaffold_11:543204-544143		
J	32	212883	N/A	-0.5504	0.7812	Aminoacyl-tRNA synthetase	scaffold_12:411614-416600		
J	32	43750	N/A	-0.5486	0.9064	-	scaffold_12:567290-569576		
J	32	203777	N/A	-0.4238	0.8309	Hypothetical mitochondrial substrate carrie	scaffold_13:1049414-1050743		
J	32	191023	N/A	-0.6061	0.857	-	scaffold_13:1093101-1094048		
J	32	54558	N/A	-0.6578	0.9749	Conserved WD40 repeat-containing protein AN11	scaffold_13:363748-365808		
J	32	57034	N/A	-1.024	1.6097	Short-chain acyl-CoA dehydrogenase	scaffold_13:374552-376462		
J	32	213282	N/A	-0.5912	0.7435	-	scaffold_13:879280-880527		
J	32	57100	N/A	-0.6096	0.7187	Mitochondrial carrier protein	scaffold_13:912746-914040		
J	32	54716	N/A	-0.3788	0.6323	Hypothetical protein with RRM domain	scaffold_14:360596-362431		
J	32	44470	N/A	-0.577	0.9025	Fungal specific transcription factor	scaffold_14:394100-396749		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	32	57159	N/A	-0.7465	0.8392	-	scaffold_14:444006-445070		
J	32	132708	N/A	-0.5819	0.84	-	scaffold_14:458379-460079		
J	32	213721	N/A	-0.3581	0.5426	-	scaffold_15:195140-196672		
J	32	128721	N/A	-0.7815	0.9344	-	scaffold_15:294514-302607		
J	32	54854	N/A	-0.4097	0.7686	Inositol-3-phosphate synthase	scaffold_16:136234-137882		
J	32	213915	N/A	-0.5412	0.7056	mRNA deadenylase subunit	scaffold_16:318322-319873		
J	32	213962	N/A	-0.4371	0.6047	Hypothetical homoserine O-acetyltransferase	scaffold_16:468013-469593		
J	32	57270	N/A	-0.5695	0.8387	-	scaffold_16:608447-611469		
J	32	214038	N/A	-0.5526	0.8636	DEAD/DEAH box helicase	scaffold_16:672902-678186		
J	32	120917	N/A	-0.4973	0.6176	-	scaffold_16:835137-836807		
J	32	204293	N/A	-0.5716	0.5989	-	scaffold_16:87161-89703		
J	32	55055	N/A	-0.6295	0.8427	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_18:106207-108695		
J	32	214562	N/A	-0.6231	0.8359	-	scaffold_18:484302-485427		
J	32	193955	N/A	-0.5038	0.7849	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_18:538798-539877		
J	32	45622	N/A	-1.0946	1.5421	-	scaffold_18:618696-619744		
J	32	45754	N/A	-0.2399	0.3889	hypothetical glutamine tRNA synthetase	scaffold_19:360321-362325		
J	32	173727	N/A	-0.62	0.927	-	scaffold_2:1127424-1129266		
J	32	174643	N/A	-0.6368	0.9275	U4/U6 small nuclear ribonucleoprotein Prp4 (contains WD40 repeats)	scaffold_2:1222314-1224406		
J	32	52342	N/A	-0.4833	0.8045	-	scaffold_2:2513761-2514867		
J	32	37318	N/A	-0.5919	0.7312	-	scaffold_2:2956336-2958547		
J	32	173461	N/A	-0.3083	0.6634	-	scaffold_2:3120814-3121959		
J	32	207321	N/A	-0.7617	1.0408	Hypothetical G-protein with WD-40 repeats	scaffold_2:3306547-3308572		
J	32	55524	N/A	-0.8281	0.9095	Hypothetical transmembrane protein	scaffold_2:586870-588505		
J	32	214877	N/A	-0.6598	1.0461	Tyrosinase	scaffold_24:85529-86144		
J	32	52614	N/A	-0.6759	0.8828	FAD-binding protein DIMINUTO	scaffold_3:1529219-1530799		
J	32	207899	N/A	-0.3689	0.4638	Major facilitator superfamily	scaffold_3:1744459-1750296		
J	32	207962	N/A	-0.502	0.6293	Splicing coactivator SRm160	scaffold_3:1899936-1902548		
J	32	175871	N/A	-0.5801	0.7264	hypothetical protein; KOG Class: General function prediction only; KOG Id: 3038; KOG description: Histone acetyltransferase SAGA associated factor SGF29	scaffold_3:1936167-1937984		
J	32	52673	N/A	-0.6399	0.7802	hogA, osmotic sensitivity mitogen-activated protein (MAP) kinase	scaffold_3:2062825-2064491		
J	32	38274	N/A	-0.7749	1.0352	-	scaffold_3:2150608-2151816		
J	32	130480	N/A	-0.8479	1.0543	Predicted RNA binding protein, contains G-patch domain	scaffold_3:2826921-2829180		
J	32	38618	N/A	-0.7108	0.9697	hypothetical transcription initiation factor	scaffold_3:3420911-3421851		
J	32	123950	N/A	-0.3244	0.3973	Protein phosphatase 2C-like	scaffold_3:3435305-3436989		
J	32	129776	N/A	-0.3688	0.4195	-	scaffold_3:3538705-3541341		
J	32	47279	N/A	-0.6669	0.8509	Autophagy protein Apg9	scaffold_3:614543-617435		
J	32	208826	N/A	-0.5523	0.9342	-	scaffold_4:1320817-1323588		
J	32	39100	N/A	-0.4298	0.6638	hypothetical Aflatoxin biosynthesis regulatory protein	scaffold_4:1414188-1416509		
J	32	126104	N/A	-0.4351	0.518	Splicing factor SPF30	scaffold_4:2062562-2063438		
J	32	209029	N/A	-0.3832	0.7974	-	scaffold_4:2473204-2474000		
J	32	53077	N/A	-0.534	0.8192	Predicted L-carnitine dehydratase/alpha-methylacyl-CoA racemase	scaffold_4:2638011-2639462		
J	32	53084	N/A	-0.2652	0.3248	Ubiquitin-conjugating enzymes, 16 kDa	scaffold_4:2686404-2687367		
J	32	56085	N/A	-0.7264	1.0472	Nicotinate-nucleotide pyrophosphorylase	scaffold_4:2815057-2816155		
J	32	209161	N/A	-0.9302	1.2387	Major facilitator superfamily	scaffold_4:2832472-2833935		
J	32	178256	N/A	-0.3854	0.6396	Related to histidine kinase	scaffold_4:305222-307381		
J	32	55954	N/A	-0.6121	0.9669	Peroxisomal biogenesis protein	scaffold_4:727174-728089		
J	32	199191	N/A	-0.5749	0.7531	Copper fist DNA-binding	scaffold_4:762682-764405		
J	32	143460	N/A	-0.6314	0.8865	Predicted H+-transporting two-sector ATPase	scaffold_5:1275605-1276539		
J	32	119764	N/A	-0.4554	0.7117	Zn-finger, C2H2 type	scaffold_5:1548061-1550963		
J	32	200187	N/A	-0.829	1.1902	pepC. Subtilisin like serine protease	scaffold_5:1563187-1564858		
J	32	200205	N/A	-0.3007	0.4506	-	scaffold_5:1602861-1608369		
J	32	200255	N/A	-0.4524	0.9553	Hypothetical cation efflux protein	scaffold_5:1735612-1736839		
J	32	56237	N/A	-0.6041	0.8618	hypothetical endoribonuclease	scaffold_5:1769951-1770669		
J	32	39623	N/A	-0.4963	0.9464	-	scaffold_5:197427-200555		
J	32	48253	N/A	-0.7348	0.9896	-	scaffold_5:229998-234020		
J	32	53121	N/A	-0.7358	0.9767	Choline transporter-like protein	scaffold_5:25489-27826		
J	32	209558	N/A	-0.7791	0.983	Phosphoglucomutase/phosphomannomutase	scaffold_5:920906-922843		
J	32	182373	N/A	-0.3602	0.597	Thioesterase superfamily	scaffold_6:1695762-1696373		
J	32	40387	N/A	-0.6064	0.9643	-	scaffold_6:403884-405299		
J	32	40493	N/A	-0.38	0.5499	-	scaffold_6:726031-727378	120	
J	32	182017	N/A	-0.4583	0.7253	Short-chain dehydrogenase/reductase	scaffold_6:729839-731041	120	
J	32	41272	N/A	-0.3887	0.7985	-	scaffold_7:1266928-1267266		
J	32	183410	N/A	-0.6321	1.003	-	scaffold_7:1375543-1376694		
J	32	210556	N/A	-0.7025	1.0553	-	scaffold_7:503844-505289		
J	32	49011	N/A	-0.338	0.6019	-	scaffold_7:609339-610667		
J	32	126465	N/A	-0.7191	0.885	-	scaffold_7:790338-791159		
J	32	49380	N/A	-0.6263	0.8444	-	scaffold_8:1111079-1113069	121	
J	32	184612	N/A	-0.478	0.6813	Inositol polyphosphate kinase	scaffold_8:1114336-1118554	121	

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
J	32	185664	N/A	-0.4751	0.7865	-	scaffold_8:1153421-1155355		
J	32	49232	N/A	-0.4751	0.5407	-	scaffold_8:244820-246739		
J	32	184507	N/A	-0.8433	1.2129	-	scaffold_8:847597-848655		
J	32	41483	N/A	-0.3774	0.5016	-	scaffold_8:97321-99230		
J	32	211361	N/A	-0.6171	0.6317	-	scaffold_9:89843-90730		
K	1	42602	N/A	0.39	-0.3512	Cytochrome P450	scaffold_10:102802-104420		
K	1	54213	N/A	0.4811	-0.4342	von Willebrand factor and related coagulation proteins	scaffold_10:1681263-1683113		
K	1	132962	N/A	0.4237	-0.3294	Fungal specific transcription factor	scaffold_11:1289571-1291037		
K	1	43449	N/A	0.4698	-0.5601	Hypothetical Cytochrome P450 monooxygenase	scaffold_11:1300361-1302141		
K	1	213409	N/A	0.4047	-0.3447	Monooxygenase, FAD-binding	scaffold_14:45850-47886		
K	1	54781	N/A	0.527	-0.5345	Uncharacterized conserved protein, contains PCI domain	scaffold_15:120819-122336		
K	1	44823	N/A	0.442	-0.3463	-	scaffold_15:535858-536589		
K	1	45027	N/A	0.3421	-0.327	-	scaffold_16:239779-240276		
K	1	37447	N/A	0.4243	-0.3444	-	scaffold_2:3380950-3381790		
K	1	38991	N/A	0.3484	-0.337	-	scaffold_4:1064465-1065188		
K	1	40148	N/A	0.3083	-0.4008	-	scaffold_5:2036400-2037283		
K	1	127572	N/A	0.3101	-0.3449	-	scaffold_5:711610-712158		
K	1	182707	N/A	0.3869	-0.3604	hypothetical chitin-binding protein	scaffold_6:1859532-1859798		
K	1	48666	N/A	0.3419	-0.3293	-	scaffold_6:555914-559257		
K	1	123664	N/A	0.3349	-0.3848	-	scaffold_6:652329-653089		
K	1	183678	N/A	0.4212	-0.6078	Major facilitator superfamily	scaffold_7:181401-182989		
K	1	41565	N/A	0.3589	-0.3366	Hypothetical protein. May be a flavin-containing monooxygenase	scaffold_8:353913-355815		
K	1	41618	N/A	0.3437	-0.3429	Hypothetical polyketide synthase	scaffold_8:489555-500948		
K	1	186225	N/A	0.4083	-0.4417	-	scaffold_9:701735-703194		
K	1	53992	N/A	0.4832	-0.4424	-	scaffold_9:933955-935018		
K	2	35369	N/A	0.2991	-0.3473	-	scaffold_1:22796-24147		
K	2	35652	N/A	0.2716	-0.3991	Fungal specific transcription factor	scaffold_1:950583-952298		
K	2	189129	N/A	0.3691	-0.4745	Cytochrome P450 similar to Aspergillus fumigatus 70982077 Cytochrome P450	scaffold_11:1430083-1431890		
K	2	192987	N/A	0.3699	-0.3962	Acyl transferase domain	scaffold_16:166878-173203		
K	2	137717	N/A	0.3804	-0.4417	-	scaffold_19:180074-180457		
K	2	37590	N/A	0.2875	-0.3355	-	scaffold_2:3830922-3831827		
K	2	47263	N/A	0.254	-0.3132	-	scaffold_3:509776-511207		
K	2	40697	N/A	0.2905	-0.3415	-	scaffold_6:1379715-1380401		
K	2	139302	N/A	0.2923	-0.4094	-	scaffold_6:1420667-1422655		
K	3	50478	N/A	0.9583	-1.1146	putative mRNA capping enzyme	scaffold_13:367117-369507		
K	3	44892	N/A	0.3471	-0.4239	-	scaffold_15:771250-771711		
K	3	175221	N/A	0.3741	-0.3289	Aromatic amino acid aminotransferase and related proteins	scaffold_2:67265-69166		
K	3	52694	N/A	0.4066	-0.4029	Possible transcription factor, DNA damage related	scaffold_3:2252004-2256616		
K	3	175881	N/A	0.5311	-0.4674	Hypothetical peptidase	scaffold_3:967312-969087		
K	3	39300	N/A	0.6274	-0.6426	-	scaffold_4:2082516-2083021		
K	3	46219	N/A	0.6136	-0.5101	Monooxygenase	scaffold_515:96-1284		
K	3	40607	N/A	0.4073	-0.4195	-	scaffold_6:1110299-1111558		
K	3	40388	N/A	0.309	-0.2892	-	scaffold_6:408181-408756		
K	3	41815	N/A	0.2891	-0.319	(pelA) extracellular pectin lyase A	scaffold_8:1082406-1083762		
K	3	202096	N/A	0.6117	-0.6244	1-acyl-sn-glycerol-3-phosphate acyltransferase	scaffold_9:1298092-1299031		
K	3	42040	N/A	0.3713	-0.3917	-	scaffold_9:50844-51938		
K	3	42283	N/A	0.5492	-0.5846	-	scaffold_9:781466-782013		
K	3	42313	N/A	0.4518	-0.4902	ABC transporter	scaffold_9:859196-861150		
K	4	142179	N/A	0.3659	-0.4211	-	scaffold_12:826521-827586		
K	4	57106	N/A	0.6669	-0.5914	-	scaffold_13:1021982-1023436		
K	4	44910	N/A	0.62	-0.3915	-	scaffold_15:820962-821267		
K	4	197459	N/A	0.4376	-0.6649	Translation initiation factor	scaffold_2:1795559-1797044		
K	4	38111	N/A	0.2754	-0.2686	-	scaffold_3:1599546-1599848		
K	4	127977	N/A	0.5241	-0.4625	-	scaffold_4:234129-234524		
K	4	180735	N/A	0.6718	-0.4931	FOG: RCC1 domain	scaffold_5:320873-324346		
K	4	121468	N/A	0.6835	-0.655	Hypothetical Glutamyl-tRNA synthetase	scaffold_6:1683949-1685530		
K	5	142765	N/A	0.3504	-0.4116	Voltage-gated shaker-like K+ channel, subunit β/KCNAB	scaffold_1:3508-4411		
K	5	46874	N/A	0.3385	-0.4013	Cytochrome P450	scaffold_1:3888125-3889921		
K	5	139484	N/A	0.5402	-0.4303	Glucose-methanol-choline oxidoreductase	scaffold_10:122040-124020		
K	5	43571	N/A	0.2919	-0.3138	-	scaffold_11:1644080-1644730		
K	5	190120	N/A	0.3861	-0.3014	putative β-lactamase	scaffold_12:1024845-1026115		
K	5	43845	N/A	0.2852	-0.3363	-	scaffold_12:840207-841190		
K	5	134931	N/A	0.3625	-0.3827	Polyprenyl synthetase	scaffold_13:43130-44229		
K	5	47351	N/A	0.303	-0.2917	oxidoreductase	scaffold_3:1053096-1054543		
K	5	48548	N/A	0.3807	-0.3853	RTA1 like protein	scaffold_5:2241857-2243930		
K	5	53362	N/A	0.3796	-0.5025	-	scaffold_5:2358978-2359677		
K	5	134447	N/A	0.7351	-0.6973	Intracellular membrane-bound Ca2+-independent phospholipase A2	scaffold_7:1047846-1049110		
K	5	40979	N/A	0.3986	-0.4539	-	scaffold_7:257139-257770		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
K	5	183599	N/A	0.4795	-0.7016	Hypothetical sulfhydryl oxidase	scaffold_7:919762-920494		
K	5	211232	N/A	0.2547	-0.2454	Thioredoxin-related	scaffold_8:1245670-1247588		
K	6	36526	N/A	0.5704	-0.4238	-	scaffold_1:3843540-3844740		
K	6	42739	N/A	0.3288	-0.3463	-	scaffold_10:552794-553105		
K	6	43264	N/A	0.559	-0.4931	-	scaffold_11:724894-725796		
K	6	43783	N/A	0.3352	-0.3069	-	scaffold_12:652309-652731		
K	6	38584	N/A	0.5832	-0.4202	-	scaffold_3:3324383-3325186		
K	6	39324	N/A	0.3214	-0.2929	Zinc-containing alcohol dehydrogenase	scaffold_4:2147576-2148710		
K	6	183972	N/A	0.3985	-0.3104	Major facilitator superfamily	scaffold_7:1438571-1440213		
K	6	42262	N/A	0.3448	-0.2405	Iron/ascorbate family oxidoreductases	scaffold_9:708426-709651		
K	7	35827	N/A	0.3811	-0.2504	-	scaffold_1:1485169-1486446		
K	7	36368	N/A	0.5714	-0.3768	-	scaffold_1:3400957-3401298		
K	7	36483	N/A	0.4853	-0.3708	-	scaffold_1:3733947-3735287		
K	7	188942	N/A	0.4914	-0.3194	hypothetical cutinase	scaffold_11:1488715-1489569		
K	7	43275	N/A	0.4388	-0.2903	Hypothetical fungal pheromone mating factor	scaffold_11:753185-754381		
K	7	189361	N/A	0.4736	-0.329	-	scaffold_12:763122-764756		
K	7	190576	N/A	0.5535	-0.3125	-	scaffold_13:716838-718083		
K	7	131509	N/A	0.6173	-0.3829	related to extracellular tannase of Aspergillus oryzae; the A. oryzae protein is apparently cleaved post-translationally into the two subunits of the enzyme	scaffold_15:866043-867749		
K	7	193061	N/A	0.5596	-0.3232	-	scaffold_16:229695-229904		
K	7	45066	N/A	0.5242	-0.3833	-	scaffold_16:347310-348315		
K	7	37488	N/A	0.4358	-0.275	-	scaffold_2:3506277-3506851		
K	7	39004	N/A	0.4971	-0.3	putative extracellular carboxylesterase	scaffold_4:1104882-1106552		
K	7	39467	N/A	0.6097	-0.4379	-	scaffold_4:2605126-2606279		
K	7	180712	N/A	0.5264	-0.354	Major facilitator superfamily	scaffold_5:2213102-2214742		
K	7	40241	N/A	0.3586	-0.3164	Intradiol ring-cleavage dioxygenase	scaffold_5:2297909-2299015		
K	7	42165	N/A	0.561	-0.3592	Hypothetical copper transporter, low affinity	scaffold_9:435751-436382		
K	8	172233	N/A	0.3462	-0.3254	Major facilitator superfamily	scaffold_1:3538486-3539943		
K	8	43302	N/A	0.5959	-0.5863	-	scaffold_11:826713-827507		
K	8	43920	N/A	0.372	-0.3596	-	scaffold_12:1084438-1085580		
K	8	44118	N/A	0.3567	-0.3429	-	scaffold_13:449739-450964		
K	8	194086	N/A	0.2829	-0.2573	Major facilitator superfamily	scaffold_19:535080-536909		
K	8	37446	N/A	0.4979	-0.4216	Basic-leucine zipper (bZIP) transcription factor	scaffold_2:3376787-3378712		
K	8	127347	N/A	0.4425	-0.3959	-	scaffold_3:463912-464430		
K	8	40704	N/A	0.412	-0.3403	related to ferro-O2-oxidoreductase of the yeast Arxula adeninivorans	scaffold_6:1399591-1402859		
K	8	184506	N/A	0.3016	-0.3734	Ankyrin	scaffold_8:1231160-1231405		
K	8	134460	N/A	0.5139	-0.5039	-	scaffold_8:729604-730779		
K	8	123678	N/A	0.3591	-0.3423	hypothetical α-1,6-mannanase	scaffold_9:808372-809503		
K	9	46505	N/A	0.4842	-0.3536	-	scaffold_1:1555582-1556454		
K	9	52082	N/A	0.5412	-0.3885	Peptidase A4, scytalidopepsin B	scaffold_1:3811393-3812241		
K	9	42622	N/A	0.3426	-0.3216	Hypothetical. Related to sporulation negative regulatory protein-like protein [M. grisea].	scaffold_10:171512-172300		
K	9	43411	N/A	0.494	-0.3197	putative extracellular protein	scaffold_11:1171392-1171888		
K	9	189194	N/A	0.4698	-0.3308	hypothetical FAD/FMN-containing dehydrogenase	scaffold_11:1304211-1305778		
K	9	131911	N/A	0.3867	-0.3354	putative carboxylesterase	scaffold_12:608361-609872		
K	9	43787	N/A	0.3122	-0.2912	-	scaffold_12:666218-667076		
K	9	44277	N/A	0.3222	-0.2399	-	scaffold_13:898678-899802		
K	9	45175	N/A	0.3921	-0.4185	-	scaffold_16:701267-702272		
K	9	57436	N/A	0.4745	-0.4437	xynA, xylanase A. extracellular GH family 11 endo-1,4-beta-xylanase	scaffold_19:419132-420626		
K	9	55212	N/A	0.4623	-0.4507	(pelD) extracellular pectin lyase D	scaffold_24:97056-98424		
K	9	46149	N/A	0.4792	-0.3526	-	scaffold_26:47930-48358		
K	9	46156	N/A	0.3375	-0.2663	-	scaffold_26:76639-77244		
K	9	177856	N/A	0.3492	-0.3332	Major facilitator superfamily	scaffold_3:1499306-1500967		
K	9	124460	N/A	0.3672	-0.3578	Hypothetical protein with RRM domain	scaffold_3:1582917-1584343		
K	9	175936	N/A	0.57	-0.3956	Naringenin-chalcone synthase	scaffold_3:337256-338248		
K	9	179052	N/A	0.4448	-0.3848	Hypothetical ubiquitin carboxyl-terminal hydrolase	scaffold_4:1199709-1200833		
K	9	39305	N/A	0.318	-0.2639	-	scaffold_4:2091278-2091883		
K	9	47920	N/A	0.5445	-0.2999	-	scaffold_4:985674-987077		
K	9	41231	N/A	0.4251	-0.4272	-	scaffold_7:1055711-1056094		
K	9	183939	N/A	0.4197	-0.3484	-	scaffold_7:1430154-1430559		
K	9	42253	N/A	0.5047	-0.3067	Major facilitator superfamily	scaffold_9:684557-686086		
K	10	43348	N/A	0.5161	-0.3423	Ribosomal protein S19e	scaffold_11:973880-974972		
K	10	50972	N/A	0.3531	-0.2701	putative extracellular tannase and feruloyl esterase	scaffold_16:234574-236193		
K	10	175329	N/A	0.4105	-0.3378	-	scaffold_2:1649231-1652198		
K	10	37389	N/A	0.4939	-0.4104	von Willebrand factor and related coagulation proteins	scaffold_2:3198401-3199489		
K	10	36752	N/A	0.4667	-0.3765	-	scaffold_2:642354-643295		
K	10	178379	N/A	0.3302	-0.2862	related to tannase	scaffold_4:1102165-1103922		
K	10	39253	N/A	0.8808	-0.5567	Acyl carrier protein (ACP)	scaffold_4:1841631-1842491		
K	10	38796	N/A	0.5068	-0.5411	-	scaffold_4:380582-381037		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
K	10	40496	N/A	0.5133	-0.3586	-	scaffold_6:734762-735991		
K	10	184329	N/A	0.4174	-0.3693	putative alkaline lipase	scaffold_7:193164-194280		
K	10	41078	N/A	0.3306	-0.2684	-	scaffold_7:584137-584526		
K	10	49373	N/A	0.4385	-0.3027	-	scaffold_8:1052681-1053580		
L	1	195878	-1.4466	N/A	N/A	Major facilitator superfamily	scaffold_1:106562-108233		
L	1	35776	-0.52	N/A	N/A	-	scaffold_1:1316618-1318427		
L	1	36034	-0.3593	N/A	N/A	-	scaffold_1:2091291-2092006		
L	1	173821	-0.574	N/A	N/A	hypothetical glutamate decarboxylase (EC 4.1.1.15)	scaffold_2:1720049-1721859		
L	1	47023	-0.4635	N/A	N/A	-	scaffold_2:1772448-1773115		
L	1	38567	-0.3611	N/A	N/A	Protein kinase	scaffold_3:3272949-3275478		
L	1	37787	-0.3228	N/A	N/A	-	scaffold_3:434291-435193		
L	1	37792	-0.6571	N/A	N/A	Haloacid dehalogenase-like hydrolase	scaffold_3:445657-446547		
L	1	38917	-0.6979	N/A	N/A	Hypothetical Flavoprotein monooxygenase	scaffold_4:846692-848158		
L	1	183782	-0.4073	N/A	N/A	Deduced protein shares amino acid sequence identity with Saccharomyces cerevisiae GCD10 gene product comprising a subunit of tRNA (1-methyladenosine) methyltransferase with Gcd14p; required for the modification of the adenine at position 58 in tRNAs, especially tRNAi-Met.	scaffold_7:1459045-1460861		
L	1	210666	-0.5221	N/A	N/A	-	scaffold_7:826583-827594		
L	1	186259	-0.6704	N/A	N/A	Major facilitator superfamily	scaffold_9:26460-28076		
L	1	42197	-0.3925	N/A	N/A	-	scaffold_9:524206-525114		
L	2	188015	-0.5241	N/A	N/A	-	scaffold_10:1917599-1918120		
L	2	175698	-0.3411	N/A	N/A	Related to arylsulfatase A and related enzymes; inorganic ion transport and metabolism; EC 3.1.6.1	scaffold_3:1295194-1296967		
L	2	37763	-0.4393	N/A	N/A	-	scaffold_3:358851-359380		
L	2	126161	-0.4531	N/A	N/A	-	scaffold_5:2168937-2169806		
L	2	40600	-0.3838	N/A	N/A	-	scaffold_6:1093541-1094524		
L	2	183892	-0.7183	N/A	N/A	CDK9 kinase-activating protein cyclin T	scaffold_7:607587-608402		
L	2	185357	-0.4657	N/A	N/A	Major facilitator superfamily	scaffold_8:904240-905948		
L	3	170270	-0.6167	N/A	N/A	Nitrilase/cyanide hydratase and apolipoprotein N-acyltransferase	scaffold_1:774950-776032		
L	3	126860	-0.3879	N/A	N/A	Hypothetical polysaccharide deacetylase	scaffold_10:1091929-1092732		
L	3	190560	-0.9804	N/A	N/A	Glucose/ribitol dehydrogenase	scaffold_13:233526-234269		
L	3	191756	-0.5791	N/A	N/A	-	scaffold_14:608625-609442		
L	3	204359	-0.4112	N/A	N/A	-	scaffold_16:336178-336762		
L	3	175855	-0.6458	N/A	N/A	Major facilitator superfamily	scaffold_3:1243760-1245283		
L	3	201918	-0.4951	N/A	N/A	Synaptic vesicle protein Synapsin	scaffold_9:377196-379796		
L	4	42932	-0.7747	N/A	N/A	Rhodopsin-like GPCR superfamily	scaffold_10:1190812-1192273		
L	4	122402	-0.35	N/A	N/A	-	scaffold_10:1863883-1865497		
L	4	42664	-0.6131	N/A	N/A	-	scaffold_10:300966-302375		
L	4	212525	-0.4388	N/A	N/A	Candidate DNA replication licensing factor	scaffold_11:664524-667213		
L	4	212837	-0.4532	N/A	N/A	UTP–glucose-1-phosphate uridylyltransferase	scaffold_12:223200-225598		
L	4	175161	-0.3847	N/A	N/A	-	scaffold_2:1728467-1729207		
L	4	174136	-0.3658	N/A	N/A	-	scaffold_2:289155-290025		
L	4	208685	-0.7246	N/A	N/A	Phosphoenolpyruvate carboxykinase, N-terminal,	scaffold_4:716275-718598		
L	4	181060	-0.4116	N/A	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae UTP4 gene product; a nucleolar protein, component of the small subunit (SSU) processome containing the U3 snoRNA that is involved in processing of pre-18S rRNA.	scaffold_5:498694-501665		
L	5	126473	-0.7029	N/A	N/A	-	scaffold_1:120721-121500		
L	5	205848	-1.2253	N/A	N/A	Sulfate/bicarbonate/oxalate exchanger SAT-1 and related transporters (SLC26 family)	scaffold_1:1772311-1775172		
L	5	36257	-0.5185	N/A	N/A	Nucleolar GTPase/ATPase p130	scaffold_1:3054590-3055849		
L	5	43369	-0.425	N/A	N/A	Major facilitator superfamily	scaffold_11:1058742-1060634		
L	5	43614	-0.8236	N/A	N/A	-	scaffold_12:119861-120841		
L	5	130434	-0.7947	N/A	N/A	Protein required for normal rRNA processing	scaffold_13:527259-529317		
L	5	44202	-0.6309	N/A	N/A	G-protein containing WD40 repeats	scaffold_13:673799-675352		
L	5	50578	-0.6048	N/A	N/A	hypothetical Cytochrome c and c1 heme-lyase	scaffold_13:813900-814769		
L	5	194355	-0.8128	N/A	N/A	Amino acid permease	scaffold_19:514258-516108		
L	5	52194	-0.4949	N/A	N/A	-	scaffold_2:1002134-1006100		
L	5	206792	-0.8649	N/A	N/A	RNA polymerase subunit	scaffold_2:1383001-1384296		
L	5	52269	-0.3961	N/A	N/A	-	scaffold_2:1628652-1632512		
L	5	36826	-0.9883	N/A	N/A	-	scaffold_2:915509-917813		
L	5	51409	-0.6268	N/A	N/A	-	scaffold_20:90344-92407		
L	5	208231	-0.7074	N/A	N/A	hypothetical Sas10/Utp3 protein; KOG Class: Chromatin structure and dynamics; KOG Id: 3118; KOG description: Disrupter of silencing SAS10	scaffold_3:2797861-2799880		
L	5	52769	-0.7224	N/A	N/A	-	scaffold_3:3004899-3006630		
L	5	52796	-0.5043	N/A	N/A	Mitochondrial import inner membrane translocase, subunit Tim44	scaffold_3:3229258-3230859		
L	5	208387	-0.492	N/A	N/A	RNA-binding protein LARP/SRO9 and related La domain proteins	scaffold_3:3248178-3250433		
L	5	199043	-0.7453	N/A	N/A	ATP Citrate lyase	scaffold_4:189886-191422		
L	5	179444	-0.825	N/A	N/A	-	scaffold_4:1985111-1986941		
L	5	179623	-0.6246	N/A	N/A	WD40 repeat protein	scaffold_4:2503147-2504946		
L	5	38790	-0.8962	N/A	N/A	Hypothetical protein.	scaffold_4:367818-369467		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
L	5	38822	-0.6426	N/A	N/A	Predicted gene product shares amino acid sequence identity with the Saccharomyces cerevisiae UTP20 gene product; a component of the small-subunit (SSU) processome, which is involved in the biogenesis of the 18S rRNA.	scaffold_4:479201-487033		
L	5	200112	-0.7214	N/A	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae UTP15 gene product; a nucleolar protein, component of the small subunit (SSU) processome containing the U3 snoRNA that is involved in processing of pre-18S rRNA.	scaffold_5:1219718-1221343		
L	5	128981	-0.5004	N/A	N/A	Sugar transporter	scaffold_5:1999478-2008712		
L	5	200680	-0.4537	N/A	N/A	Eukaryotic translation initiation factor 3, subunit 7	scaffold_6:1011873-1013698		
L	5	48843	-0.7488	N/A	N/A	rRNA processing protein	scaffold_6:1605393-1610979		
L	5	40884	-0.9642	N/A	N/A	Hypothetical nitric-oxide synthase (EC 1.14.13.39)	scaffold_6:1976933-1980231		
L	5	40381	-0.4263	N/A	N/A	related to Mtop1 protein of budding yeast which in complex with Mssp1 is involved in translation optimization of mitochondria	scaffold_6:288765-290927		
L	5	53574	-0.4375	N/A	N/A	Candidate carbamoyl-phosphate synthase	scaffold_7:335601-339352		
L	5	53910	-0.9348	N/A	N/A	Fatty acid desaturase	scaffold_8:1670762-1672102		
L	5	46180	-0.6772	N/A	N/A	Hypothetical protein. Contains a DNA helicase motif	scaffold_89:6578-7716		
L	5	49726	-0.6406	N/A	N/A	Related to the IMP3 gene product of Saccharomyces cerevisiae comprising a component of the SSU processome, which is required for pre-18S rRNA processing	scaffold_9:1391781-1392432		
L	5	186735	-0.6062	N/A	N/A	-	scaffold_9:31869-33662		
M	1	120082	0.488	N/A	N/A	Predicted hydrolase involved in interstrand cross-link repair	scaffold_1:2980813-2983412		
M	1	55462	0.5752	N/A	N/A	-	scaffold_1:3037587-3039008		
M	1	187454	0.5608	N/A	N/A	-	scaffold_10:26621-28010		
M	1	143984	0.9453	N/A	N/A	-	scaffold_1106:210-992		
M	1	44122	0.4393	N/A	N/A	-	scaffold_13:462471-463397		
M	1	191646	0.3832	N/A	N/A	Generic methyltransferase	scaffold_14:654005-655512		
M	1	184264	0.4776	N/A	N/A	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_7:112037-113828		
M	1	211341	0.4392	N/A	N/A	-	scaffold_8:1705310-1705989		
M	2	172796	0.6738	N/A	N/A	Hypothetical urea amidolyase	scaffold_1:314688-318870		
M	2	187486	0.4957	N/A	N/A	-	scaffold_10:1699732-1701822		
M	2	43903	0.5315	N/A	N/A	-	scaffold_12:1034052-1036079		
M	2	203401	0.4327	N/A	N/A	Amidase	scaffold_12:1072782-1074567		
M	2	206422	2.0334	N/A	N/A	Monocarboxylate transporter	scaffold_2:33809-35071		
M	2	38707	0.5041	N/A	N/A	Ferric reductase like transmembrane component	scaffold_4:111615-114324		
M	2	48389	3.0569	N/A	N/A	Predicted transporter (major facilitator superfamily	scaffold_5:1042873-1044814		
M	2	210117	0.5373	N/A	N/A	-	scaffold_6:680388-681252		
M	2	41013	0.6117	N/A	N/A	-	scaffold_7:383074-384079		
M	3	42808	0.4757	N/A	N/A	-	scaffold_10:771780-774152		
M	3	45558	0.3933	N/A	N/A	von Willebrand factor and related coagulation proteins	scaffold_18:400653-402601		
M	3	140966	0.6342	N/A	N/A	Vesicular amine transporter	scaffold_4:175061-176758		
M	3	53656	1.2937	N/A	N/A	-	scaffold_7:962507-962911		
M	3	41975	0.4773	N/A	N/A	-	scaffold_8:1593499-1594520		
M	3	54038	0.4907	N/A	N/A	-	scaffold_9:1390349-1391122		
M	4	36425	1.1266	N/A	N/A	-	scaffold_1:3556753-3558489		
M	4	54378	0.9071	N/A	N/A	related to α-1,3-glucan synthase	scaffold_11:1006988-1014520		
M	4	44378	0.3859	N/A	N/A	-	scaffold_14:68347-68700		
M	4	52773	1.6244	N/A	N/A	ABC transporter, transmembrane region	scaffold_3:3054456-3059811		
M	4	127812	0.4815	N/A	N/A	Cutinase	scaffold_4:87167-87972		
M	4	209460	0.6734	N/A	N/A	ABC transporter	scaffold_5:636999-639174		
M	4	48688	0.6211	N/A	N/A	adenosylmethionine-8-amino-7-oxononanoate transaminase	scaffold_6:640755-643425		
M	4	49586	0.8411	N/A	N/A	-	scaffold_9:547901-548689		
M	5	35422	0.7176	N/A	N/A	Fungal transcriptional regulatory protein, N-terminal	scaffold_1:184811-186693		
M	5	50241	6.7286	N/A	N/A	Flavoprotein monooxygenase	scaffold_11:1568987-1570201	122	
M	5	189060	5.7952	N/A	N/A	Hypothetical epimerase	scaffold_11:1574643-1575481	122	
M	5	43553	4.2511	N/A	N/A	-	scaffold_11:1581694-1582477		
M	5	142301	1.3309	N/A	N/A	-	scaffold_11:1595863-1597078		
M	5	48443	1.3844	N/A	N/A	-	scaffold_5:1417862-1419099		
M	6	43480	0.7293	N/A	N/A	-	scaffold_11:1383770-1385191		
M	6	43182	1.2246	N/A	N/A	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_11:391880-393976		
M	6	44375	0.7247	N/A	N/A	-	scaffold_14:58979-60400		
M	6	45767	0.978	N/A	N/A	-	scaffold_19:398251-398742		
M	6	199018	0.6513	N/A	N/A	candidate O-methyltransferase	scaffold_4:70887-72286		
M	6	180718	0.7075	N/A	N/A	AAA+-type ATPase	scaffold_5:1437218-1439584		
M	6	125691	0.8412	N/A	N/A	-	scaffold_7:109305-110078		
M	6	53797	0.4886	N/A	N/A	related to endoglucanase of Trichoderma reesei; glucan 1,4-beta-glucosidase; cellulose-binding region; glycoside hydrolase, family 61	scaffold_8:675326-676579		
N	1	196273	N/A	-0.4849	N/A	-	scaffold_1:1518712-1519594		
N	1	36104	N/A	-0.6234	N/A	Shares amino acid sequence identity with yeast DIP2 gene product, specifically associated with the U3 snoRNA, part of the large ribonucleoprotein complex known as the small subunit (SSU) processome, required for 18S rRNA biogenesis, part of the active pre-rRNA processing complex.	scaffold_1:2316772-2319797		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	1	36184	N/A	-0.7774	N/A	hypothetical protein containing Zn-finger, C2H2 type domain.	scaffold_1:2762683-2764463		
N	1	171090	N/A	-0.6877	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae UTP14 gene product; a nucleolar protein, component of the small subunit (SSU) processome containing the U3 snoRNA that is involved in processing of pre-18S rRNA.	scaffold_1:3103139-3106148		
N	1	52046	N/A	-0.9939	N/A	Shares amino acid sequence identity with Saccharomyes cerevisiae EBP2 encoding an essential protein required for the maturation of 25S rRNA and 60S ribosomal subunit assembly; localizes to the nucleolus; constituent of 66S pre-ribosomal particles.	scaffold_1:3326141-3327324		
N	1	46885	N/A	-0.5447	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae TRM1 gene product; tRNA methyltransferase, localizes to both the nucleus and mitochondrion (yeast) to produce the modified base N2,N2-dimethylguanosine in tRNAs in both compartments	scaffold_1:3925366-3927438		
N	1	35512	N/A	-0.6831	N/A	Hypothetical. Identity with S. cerevisiae SDA1; highly conserved nuclear protein required for actin cytoskeleton organization and passage through start, plays a critical role in G1	scaffold_1:477213-479684		
N	1	130294	N/A	-0.5861	N/A	Hypothetical ATP-dependent RNA helicase	scaffold_1:494260-496804		
N	1	196062	N/A	-0.3125	N/A	Deduced translation product shares amino acid sequence identity with the Saccharomyces cerevisiae NOP1 gene product; a nucleolar protein, component of the small subunit processome complex, which is required for processing of pre-18S rRNA; has similarity to mammalian fibrillarin.	scaffold_1:744138-745384		
N	1	139419	N/A	-0.6755	N/A	KRR1-interacting protein involved in 40S ribosome biogenesis	scaffold_10:1008607-1010476		
N	1	137492	N/A	-0.3621	N/A	-	scaffold_10:1015680-1016234		
N	1	54204	N/A	-0.6462	N/A	Shares amino acid sequence identity with the Saccharomyces cerevisiae RRP3 gene product; a protein involved in rRNA processing; required for maturation of the 35S primary transcript of pre-rRNA and for cleavage leading to mature 18S rRNA; homologous to eIF-4a, which is a DEAD box RNA-dependent ATPase with helicase activity.	scaffold_10:1203477-1205032		
N	1	120052	N/A	-0.9382	N/A	Related to SPB1	scaffold_10:447199-449715		
N	1	43122	N/A	-0.6783	N/A	Hypothetical. Sequence similarity to S cerevisiae RRP15; Nucleolar, constituent of pre-60S ribosomal particles; required for processing of the 27S pre-rRNA	scaffold_11:213799-214665		
N	1	56906	N/A	-0.5667	N/A	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae PWP2 gene product; conserved 90S pre-ribosomal component essential for proper endonucleolytic cleavage of the 35 S rRNA precursor at A0, A1, and A2 sites; contains eight WD-repeats.	scaffold_11:461027-464002		
N	1	203423	N/A	-0.7063	N/A	-	scaffold_12:1154242-1155573		
N	1	138298	N/A	-0.638	N/A	Fungal transcriptional regulatory protein,	scaffold_12:585299-585478		
N	1	44347	N/A	-0.648	N/A	Ribosomal protein L3	scaffold_13:1182232-1183229		
N	1	130844	N/A	-0.772	N/A	Hypothetical protein. Appears to encode a member of the Mpp10p superfamily of proteins; component of the SSU processome, which is required for pre-18S rRNA processing, interacts with and controls the stability of Imp3p and Imp4p, essential for viability; similar to human Mpp10p.	scaffold_13:1202702-1204702		
N	1	44156	N/A	-0.3712	N/A	Related to mitochondrial translation elongation factor	scaffold_13:543221-545844		
N	1	190605	N/A	-0.4454	N/A	-	scaffold_13:684500-685003		
N	1	50549	N/A	-0.7836	N/A	Hypothetical. G-protein. WD40 repeat-containing	scaffold_13:690045-691637		
N	1	50719	N/A	-0.7282	N/A	-	scaffold_14:467482-468278		
N	1	137217	N/A	-0.8285	N/A	-	scaffold_15:190343-191071		
N	1	44755	N/A	-0.7109	N/A	-	scaffold_15:320185-322050		
N	1	51057	N/A	-0.4503	N/A	Related to Elongator complex protein, Elp3p	scaffold_16:709119-710899		
N	1	51089	N/A	-0.2848	N/A	-	scaffold_16:858991-860625		
N	1	214286	N/A	-0.4785	N/A	Predicted gene product shares limited amino acid sequence identity with the Saccharomyces cerevisiae UTP5 gene product; a nucleolar protein, component of the small subunit (SSU) processome containing the U3 snoRNA that is involved in processing of pre-18S rRNA.	scaffold_17:352563-355158		
N	1	193903	N/A	-0.499	N/A	Predicted nucleolar protein involved in ribosome biogenesis	scaffold_18:490849-492618		
N	1	36871	N/A	-0.7769	N/A	putative midasin, the largest ORF found in yeast that is believed to play a role in nuclear protein folding	scaffold_2:1088761-1103558		
N	1	137394	N/A	-0.5048	N/A	Ribosomal protein L16	scaffold_2:1121366-1122075		
N	1	206931	N/A	-0.3759	N/A	FOG: RCC1 domain	scaffold_2:1717822-1719552		
N	1	37068	N/A	-0.7579	N/A	GTPase/ATPase p130	scaffold_2:1777115-1778380		
N	1	37241	N/A	-0.3522	N/A	-	scaffold_2:2657415-2660117		
N	1	55529	N/A	-0.3391	N/A	Candidate ATP-dependent RNA helicase of the DEAD-box protein family	scaffold_2:663437-669814		
N	1	45864	N/A	-0.6935	N/A	Deduced gene product shares amino acid sequence identity with the Saccharomyces cerevisiae NIP7 gene product; a nucleolar protein required for 60S ribosome subunit biogenesis, constituent of 66S pre-ribosomal particles.	scaffold_20:89343-90077		
N	1	195098	N/A	-0.757	N/A	-	scaffold_21:56191-57292		
N	1	47358	N/A	-0.5851	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae UTP10 gene product; a nucleolar protein, component of the small subunit (SSU) processome containing the U3 snoRNA that is involved in processing of pre-18S rRNA.	scaffold_3:1123039-1128653		
N	1	176941	N/A	-0.5273	N/A	RNA polymerase	scaffold_3:1765688-1770933		
N	1	38235	N/A	-0.571	N/A	U3 small nucleolar ribonucleoprotein (snoRNP)	scaffold_3:2018829-2020002		
N	1	52705	N/A	-0.3839	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae TUF1 gene product; mitochondrial translation elongation factor Tu.	scaffold_3:2368924-2370510		
N	1	38467	N/A	-0.5051	N/A	CAATT-binding transcription factor/60S ribosomal subunit biogenesis protein	scaffold_3:2928390-2931915		
N	1	38620	N/A	-0.5691	N/A	-	scaffold_3:3424527-3426675		
N	1	39268	N/A	-0.3464	N/A	Fungal specific transcription factor	scaffold_4:1968038-1970239		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	1	39541	N/A	-0.7874	N/A	Predicted protein shares amino acid sequence identity with the Saccharomyces cerevisiae UTP22 gene product; a possible U3 snoRNP protein involved in maturation of pre-18S rRNA, based on computational analysis of large-scale protein-protein interaction data.	scaffold_4:2890338-2893688		
N	1	55936	N/A	-0.6382	N/A	Related to N. crassa RNA polymerase, β subunit	scaffold_4:462450-466293		
N	1	39937	N/A	-0.3141	N/A	-	scaffold_5:1254161-1255892		
N	1	209822	N/A	-0.7121	N/A	Hypothetical ribosomal protein L1	scaffold_5:1852718-1854071		
N	1	40169	N/A	-0.4994	N/A	-	scaffold_5:2100710-2101306		
N	1	180130	N/A	-0.6701	N/A	-	scaffold_5:2315525-2317570		
N	1	53197	N/A	-0.4663	N/A	Hypothetical IMP dehydrogenase	scaffold_5:603429-605344		
N	1	180504	N/A	-0.6168	N/A	-	scaffold_5:828766-829815		
N	1	209255	N/A	-0.3879	N/A	Mitochondrial substrate carrier	scaffold_5:87318-88597		
N	1	56339	N/A	-1.1515	N/A	Related to sulphate permease. Has 11 transmembrane domains and several sulphate transporter domains.	scaffold_6:1191276-1193802		
N	1	182540	N/A	-0.2653	N/A	-	scaffold_6:1851779-1852783		
N	1	210073	N/A	-0.9159	N/A	-	scaffold_6:510162-511299		
N	1	56429	N/A	-0.4568	N/A	-	scaffold_7:502737-503339		
N	1	49025	N/A	-0.3383	N/A	3’-5’ exonuclease	scaffold_7:678478-680826		
N	1	183221	N/A	-0.9527	N/A	-	scaffold_7:895842-896487		
N	1	184148	N/A	-0.544	N/A	-	scaffold_7:928795-930504		
N	1	53893	N/A	-0.3583	N/A	Phosphatidylethanolamine binding protein	scaffold_8:1510122-1511443		
N	1	185199	N/A	-0.6238	N/A	-	scaffold_8:341213-342271		
N	2	202528	N/A	-0.3597	N/A	related to zinc finger protein, possible Myb, DNA binding protein	scaffold_10:1072820-1075612		
N	2	211915	N/A	-0.5462	N/A	Ribosomal protein L23	scaffold_10:678709-679515		
N	2	50457	N/A	-0.6884	N/A	Nuclear GTP binding protein	scaffold_13:254028-256197		
N	2	131206	N/A	-0.5012	N/A	Nitrilase/cyanide hydratase and apolipoprotein	scaffold_15:907766-909507		
N	2	135680	N/A	-0.2878	N/A	Methyltransferases	scaffold_17:272241-273149		
N	2	45660	N/A	-0.6996	N/A	Hypothetical protein, Myb superfamily	scaffold_19:82084-83724		
N	2	173093	N/A	-0.3424	N/A	-	scaffold_2:2886827-2888497		
N	2	126121	N/A	-0.5269	N/A	Uncharacterized conserved protein related to ribosomal protein S8E	scaffold_2:3229011-3229839		
N	2	47150	N/A	-0.3964	N/A	C1-tetrahydrofolate synthase	scaffold_2:3400280-3403346		
N	2	197959	N/A	-0.6202	N/A	Hypothetical. Sequence identity with S cerevisiae NOP53 gene (nuclear); involved in biogenesis of 60S subunit of ribosome.	scaffold_2:3753040-3755850		
N	2	198660	N/A	-0.5031	N/A	Hypothetical translocase of outer mitochondrial membrane complex	scaffold_3:2624257-2625174		
N	2	47753	N/A	-0.3252	N/A	Hypothetical Metal dependent protein hydrolase	scaffold_3:3516328-3517509		
N	2	40066	N/A	-0.4541	N/A	Nuclear mRNA export factor receptor	scaffold_5:1728762-1732183		
N	2	39817	N/A	-0.506	N/A	Hypothetical glutathione-dependent formaldehyde-activating protein	scaffold_5:895277-895933		
N	2	41281	N/A	-1.0123	N/A	Predicted dehydrogenase	scaffold_7:1293594-1294535		
N	2	210935	N/A	-0.3501	N/A	Candidate eukaryotic translation initiation factor 3	scaffold_8:288669-291355		
N	2	119995	N/A	-0.4872	N/A	UDP-glucuronosyl and UDP-glucosyl transferase	scaffold_9:654741-657464		
N	3	190033	N/A	-0.6091	N/A	putative proline racemase	scaffold_12:1134032-1135234		
N	3	44271	N/A	-0.329	N/A	Related to A. nidulans radC (rad52)	scaffold_13:884129-886026		
N	3	129111	N/A	-0.488	N/A	Hydantoinase/oxoprolinase	scaffold_15:523622-527808		
N	3	128357	N/A	-0.2998	N/A	Protein kinase	scaffold_17:53006-53242		
N	3	45822	N/A	-0.5411	N/A	Major facilitator superfamily	scaffold_19:567300-568648		
N	3	47077	N/A	-0.4463	N/A	oxidoreductase	scaffold_2:2598168-2599515		
N	3	36659	N/A	-0.3858	N/A	Flavoprotein monooxygenase	scaffold_2:285406-287045		
N	3	37302	N/A	-0.4818	N/A	-	scaffold_2:2888919-2891164		
N	3	37635	N/A	-0.3702	N/A	Fungal specific transcription factor	scaffold_2:3969697-3971849		
N	3	179747	N/A	-0.8544	N/A	3-methyl-2-oxobutanoate hydroxymethyltransferase (Ketopantoate hydroxymethyltransferase).	scaffold_4:1769559-1770667		
N	3	128077	N/A	-0.6139	N/A	Putative GH family 43	scaffold_5:1315066-1315599		
N	3	143487	N/A	-0.6876	N/A	Serine/threonine protein kinase	scaffold_5:1528958-1529489		
N	3	181530	N/A	-0.3588	N/A	-	scaffold_5:1762211-1765615		
N	3	48679	N/A	-0.6519	N/A	Glutamine synthetase	scaffold_6:602736-604392		
N	3	184867	N/A	-0.2783	N/A	Nucleic acid-binding OB-fold	scaffold_8:1216992-1217747		
N	3	124843	N/A	-0.598	N/A	-	scaffold_8:1633049-1634086		
N	3	41696	N/A	-0.4523	N/A	Amidohydrolase	scaffold_8:720745-722317		
N	3	42329	N/A	-0.3047	N/A	Fungal transcriptional regulatory protein	scaffold_9:907301-909202		
N	4	171067	N/A	-0.5248	N/A	Zn-finger, GATA type	scaffold_1:1680471-1681951		
N	4	51883	N/A	-0.6575	N/A	Cyclin	scaffold_1:1869666-1871215		
N	4	172075	N/A	-0.4542	N/A	Hypothetical enoyl-CoA hydratase (EC 4.2.1.17)	scaffold_1:2109419-2110581		
N	4	172477	N/A	-0.5861	N/A	Short-chain dehydrogenase/reductase	scaffold_1:265811-266732		
N	4	51714	N/A	-0.4434	N/A	Helicase-like transcription factor HLTF/DNA helicase RAD5, DEAD-box superfamily	scaffold_1:339433-342916		
N	4	36522	N/A	-1.0598	N/A	-	scaffold_1:3832770-3833348		
N	4	35545	N/A	-0.6067	N/A	-	scaffold_1:625433-626239		
N	4	51779	N/A	-1.1891	N/A	-	scaffold_1:959794-960123		
N	4	35661	N/A	-0.4076	N/A	Fungal transcriptional regulatory protein,	scaffold_1:970984-973704		
N	4	42642	N/A	-0.4734	N/A	Ketopantoate reductase	scaffold_10:221752-222783		
N	4	42852	N/A	-0.3642	N/A	Survival protein SurE	scaffold_10:948842-950110		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	4	54298	N/A	-1.1976	N/A	hypothetical. Heterogeneous nuclear ribonucleoproteins A2/B1	scaffold_11:186947-187785		
N	4	43351	N/A	-0.8308	N/A	-	scaffold_11:988995-990417		
N	4	212814	N/A	-0.6548	N/A	Serine/threonine protein kinase	scaffold_12:163859-165961		
N	4	212833	N/A	-0.6954	N/A	putative heat shock protein Sti1	scaffold_12:209089-210553		
N	4	43791	N/A	-1.1025	N/A	Generic methyltransferase	scaffold_12:673878-674690		
N	4	190197	N/A	-0.5376	N/A	(apsC) aminopeptidase C.	scaffold_13:478566-480668		
N	4	44252	N/A	-0.4304	N/A	Dual specificity protein phosphatase	scaffold_13:829639-831145		
N	4	54817	N/A	-0.8124	N/A	Hypothetical oligopeptide transporter	scaffold_15:451128-453913		
N	4	192711	N/A	-0.4856	N/A	-	scaffold_16:486461-487482		
N	4	214216	N/A	-0.5911	N/A	Calmodulin	scaffold_17:139184-140074		
N	4	37295	N/A	-0.602	N/A	ABC transporter	scaffold_2:2871771-2876264		
N	4	194902	N/A	-0.7466	N/A	-	scaffold_21:268298-269543		
N	4	136267	N/A	-0.8469	N/A	Kinesin light chain	scaffold_21:95577-96104		
N	4	176277	N/A	-0.3794	N/A	RNA-directed RNA polymerase QDE-1 required for posttranscriptional gene silencing and RNA interference	scaffold_3:1317055-1320864		
N	4	38060	N/A	-0.5122	N/A	-	scaffold_3:1327341-1328353		
N	4	176012	N/A	-0.4149	N/A	-	scaffold_3:2092657-2093158		
N	4	38373	N/A	-0.4222	N/A	hypothetical protein; KOG Class: Chromatin structure and dynamics	scaffold_3:2626181-2628099		
N	4	39299	N/A	-0.5076	N/A	Hypothetical. Putative protein kinase domain	scaffold_4:2079631-2080719		
N	4	38953	N/A	-0.7866	N/A	Short-chain dehydrogenase/reductase	scaffold_4:943009-943997		
N	4	53269	N/A	-0.944	N/A	-	scaffold_5:1301913-1307115		
N	4	53274	N/A	-1.5203	N/A	-	scaffold_5:1336328-1337368		
N	4	127639	N/A	-0.9471	N/A	-	scaffold_5:1941794-1942453		
N	4	181107	N/A	-0.3389	N/A	NB-ARC	scaffold_5:2064392-2068195		
N	4	40161	N/A	-1.4141	N/A	-	scaffold_5:2078605-2080354		
N	4	181429	N/A	-0.3516	N/A	-	scaffold_5:2097144-2098650		
N	4	53357	N/A	-0.9004	N/A	Related to aldehyde dehydrogenase (EC 1.2.1.3). Sequence similarity to ALD2 of C. albicans	scaffold_5:2274916-2276538		
N	4	53209	N/A	-0.5178	N/A	Nsp1-like, C-terminal	scaffold_5:686530-688769		
N	4	210224	N/A	-0.8076	N/A	Histidine acid phosphatase	scaffold_6:1118900-1120642		
N	4	40691	N/A	-0.7468	N/A	hypothetical Aflatoxin biosynthesis regulatory protein	scaffold_6:1361471-1363222		
N	4	40328	N/A	-0.5147	N/A	Predicted membrane protein	scaffold_6:146296-148600		
N	4	56327	N/A	-0.526	N/A	Ubiquitin-conjugating enzyme	scaffold_6:869224-871121		
N	4	40553	N/A	-0.5027	N/A	-	scaffold_6:918054-918497		
N	4	56475	N/A	-1.1089	N/A	Aldo/keto reductase	scaffold_7:1278518-1279567		
N	4	41439	N/A	-0.5569	N/A	-	scaffold_7:1772545-1773693		
N	4	41939	N/A	-0.6522	N/A	-	scaffold_8:1473633-1474625		
N	4	185582	N/A	-0.8951	N/A	putative carboxylesterase, type B	scaffold_8:1678057-1679738		
N	4	56548	N/A	-0.6384	N/A	Generic methyltransferase	scaffold_8:416108-417374		
N	4	41724	N/A	-0.5671	N/A	-	scaffold_8:804627-805157		
N	4	185070	N/A	-0.3776	N/A	TPR-containing protein	scaffold_8:882894-884868		
N	4	137209	N/A	-0.5348	N/A	Protein kinase	scaffold_84:2-1070		
N	4	186860	N/A	-0.5111	N/A	Aminotransferase class-III	scaffold_9:846641-847969		
N	5	36472	N/A	-0.4515	N/A	-	scaffold_1:3701969-3705302		
N	5	196101	N/A	-0.5966	N/A	Formyl transferase	scaffold_1:887955-888806		
N	5	50199	N/A	-0.2589	N/A	hypothetical Oxidoreductase	scaffold_11:1265066-1266185		
N	5	212490	N/A	-0.2832	N/A	Cell division/GTP binding protein	scaffold_11:464574-466094		
N	5	189726	N/A	-0.2783	N/A	-	scaffold_12:616294-617544		
N	5	191072	N/A	-0.4858	N/A	Major facilitator superfamily permease	scaffold_13:525416-526890		
N	5	126978	N/A	-0.5745	N/A	-	scaffold_14:210891-211707		
N	5	129269	N/A	-0.6048	N/A	-	scaffold_15:528729-532827		
N	5	207079	N/A	-0.8861	N/A	Zinc-binding oxidoreductase	scaffold_2:2391048-2392097		
N	5	37354	N/A	-0.3924	N/A	Hypothetical copper amine oxidase (EC 1.4.3.6)	scaffold_2:3087189-3089185		
N	5	197786	N/A	-0.3431	N/A	(dapB) dipeptidylpeptidase	scaffold_2:3194789-3197635		
N	5	38093	N/A	-0.4704	N/A	hydrogenase activity (alcohol and 2,3-butadiol)	scaffold_3:1546948-1548231		
N	5	207996	N/A	-0.6211	N/A	Permeases for cytosine/purines, uracil, thiamine, allantoin	scaffold_3:1969189-1971203		
N	5	39501	N/A	-0.4196	N/A	-	scaffold_4:2718394-2720430		
N	5	55950	N/A	-0.3369	N/A	Related to mannose-1-phosphate guanyltransferase. [EC:2.7.7.13]	scaffold_4:674642-676193		
N	5	38879	N/A	-0.6676	N/A	hypothetical protein predicted to be an mRNA capping enzyme and a generic methyltransferase; KOG Class: RNA processing and modification ; KOG Id: 1975; KOG description: mRNA cap methyltransferase	scaffold_4:706048-708294		
N	5	183269	N/A	-0.5377	N/A	-	scaffold_7:1331073-1332125		
N	5	200887	N/A	-0.8581	N/A	Hypothetical S-adenosylmethionine-dependent methyltransferase activity	scaffold_7:143463-144365		
N	5	201083	N/A	-0.3699	N/A	Phosphatidylinositol transfer protein SEC14	scaffold_7:664175-665364		
N	5	185983	N/A	-0.4128	N/A	NADH:flavin oxidoreductase/NADH oxidase	scaffold_9:1393003-1394493		
N	6	51813	N/A	-0.823	N/A	Amino acid/polyamine transporter	scaffold_1:1300306-1302092		
N	6	172112	N/A	-0.5742	N/A	-	scaffold_1:2295271-2297250		
N	6	55447	N/A	-0.697	N/A	Regulatory protein abaA, involved in development, incl condiophores. Regulates brlA, wetA	scaffold_1:2932148-2934620		
N	6	170512	N/A	-0.7154	N/A	-	scaffold_1:2993887-2994901		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	6	55476	N/A	-0.8396	N/A	-	scaffold_1:3230337-3232733		
N	6	36332	N/A	-0.5825	N/A	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae POP4 gene product; a subunit of both RNase MRP, which cleaves pre-rRNA, and nuclear RNase P, which cleaves tRNA precursors to generate mature 5′ ends; binds to the RPR1 RNA subunit in Rnase P.	scaffold_1:3302255-3303048		
N	6	137960	N/A	-0.7076	N/A	-	scaffold_1:3595923-3596320		
N	6	55511	N/A	-0.4693	N/A	Beta-ketoacyl synthase	scaffold_1:3927879-3933576		
N	6	35666	N/A	-0.6118	N/A	FAD linked oxidase	scaffold_1:986068-987879		
N	6	186889	N/A	-0.3731	N/A	-	scaffold_10:278648-280154		
N	6	49810	N/A	-0.6942	N/A	Pantoate-beta-alanine ligase	scaffold_10:394535-395572		
N	6	43740	N/A	-0.5174	N/A	Acyl transferase region	scaffold_12:533508-539247		
N	6	54433	N/A	-1.0076	N/A	Hypothetical protein containing WD40 repeat	scaffold_12:5669-8573		
N	6	44313	N/A	-0.6886	N/A	-	scaffold_13:1058046-1059826		
N	6	50479	N/A	-0.2773	N/A	-	scaffold_13:370262-373645		
N	6	213169	N/A	-0.7092	N/A	GHMP kinase	scaffold_13:618542-620161		
N	6	191145	N/A	-0.5022	N/A	Esterase/lipase/thioesterase	scaffold_14:195362-196578		
N	6	44704	N/A	-0.4741	N/A	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae PAP2 gene product; the catalytic subunit of TRAMP (Trf4/Pap2p-Mtr4p-Air1p/2p), a nuclear poly (A) polymerase complex involved in RNA quality control; catalyzes polyadenylation of unmodified tRNAs, and snoRNA and rRNA precursors; disputed role as a DNA polymerase (yeast).	scaffold_15:163933-166088		
N	6	213643	N/A	-0.7104	N/A	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae PXR1 gene product; a protein involved in rRNA and snoRNA maturation.	scaffold_15:17321-18236		
N	6	44895	N/A	-0.9001	N/A	-	scaffold_15:777319-778452		
N	6	193196	N/A	-0.745	N/A	-	scaffold_17:237364-238141		
N	6	45258	N/A	-0.466	N/A	-	scaffold_17:39299-40084		
N	6	45546	N/A	-0.6017	N/A	CDP-alcohol phosphatidyltransferase	scaffold_18:360217-361492		
N	6	173434	N/A	-0.4553	N/A	Sec34-like protein	scaffold_2:1714927-1717513		
N	6	207002	N/A	-0.7425	N/A	Hypothetical. InterPro suggests role in chromosome condensation	scaffold_2:1880496-1882255		
N	6	175016	N/A	-0.4087	N/A	FAD linked oxidase	scaffold_2:2025848-2027560		
N	6	37407	N/A	-0.5556	N/A	-	scaffold_2:3255889-3257579		
N	6	36770	N/A	-0.4028	N/A	Major facilitator superfamily	scaffold_2:723687-725393		
N	6	52164	N/A	-0.3063	N/A	Putative RNA polymerase II regulator	scaffold_2:754702-756280		
N	6	51430	N/A	-0.6911	N/A	Shares amino acid sequence identity with Saccharomyces cerevisiae ESF2 encoding an essential nucleolar protein involved in pre-18S rRNA processing; component of the small subunit (SSU) processome.	scaffold_20:183739-184785		
N	6	46039	N/A	-0.6166	N/A	-	scaffold_21:277124-278107		
N	6	46107	N/A	-0.5808	N/A	-	scaffold_24:31450-32826		
N	6	52740	N/A	-0.5654	N/A	Myosin class II heavy chain	scaffold_3:2758754-2764951		
N	6	38600	N/A	-0.6405	N/A	Hypothetical Component of vacuolar transporter chaperone (Vtc) involved in vacuole fusion	scaffold_3:3374727-3375159	123	
N	6	52811	N/A	-0.6107	N/A	hypothetical glycoside hydrolase, family 5	scaffold_3:3375548-3376708	123	
N	6	47341	N/A	-0.5391	N/A	-	scaffold_3:954761-956196		
N	6	179409	N/A	-0.3533	N/A	-	scaffold_4:1338709-1339059		
N	6	56014	N/A	-0.6429	N/A	-	scaffold_4:1733590-1734417		
N	6	38729	N/A	-0.4667	N/A	Hypothetical. Related to RNase P	scaffold_4:183642-184367		
N	6	39280	N/A	-0.5429	N/A	Zinc-containing alcohol dehydrogenase	scaffold_4:2003657-2004658		
N	6	47806	N/A	-0.5241	N/A	-	scaffold_4:250661-252067		
N	6	178591	N/A	-0.7678	N/A	-	scaffold_4:2561226-2561998		
N	6	38906	N/A	-0.5773	N/A	-	scaffold_4:815513-816940		
N	6	39857	N/A	-0.7984	N/A	-	scaffold_5:1019658-1020400		
N	6	40013	N/A	-0.822	N/A	Protein kinase	scaffold_5:1539825-1541254		
N	6	40078	N/A	-0.6235	N/A	Predicted metalloprotease with chaperone activity	scaffold_5:1767368-1769499		
N	6	126952	N/A	-0.541	N/A	-	scaffold_5:1925001-1925554	124	
N	6	209830	N/A	-1.4217	N/A	hypothetical FAD/FMN-containing dehydrogenase	scaffold_5:1928719-1930476	124	
N	6	180515	N/A	-0.6526	N/A	Major facilitator superfamily	scaffold_5:624185-625559		
N	6	53381	N/A	-0.4837	N/A	cytochrome b5 domain	scaffold_6:111882-112811		
N	6	40757	N/A	-0.5802	N/A	-	scaffold_6:1562995-1564377		
N	6	53517	N/A	-0.9282	N/A	-	scaffold_6:1653030-1653416		
N	6	48610	N/A	-0.3808	N/A	-	scaffold_6:185029-188961		
N	6	41555	N/A	-1.0128	N/A	-	scaffold_8:330636-331990		
N	6	41604	N/A	-0.7754	N/A	Protein of unknown function (DUF455)	scaffold_8:454324-455706		
N	6	186804	N/A	-0.6142	N/A	-	scaffold_9:101942-102469		
N	6	42523	N/A	-0.8062	N/A	Hypothetical Inositol monophosphatase	scaffold_9:1522738-1523835		
N	6	42536	N/A	-0.6832	N/A	-	scaffold_9:1577550-1581451		
N	6	211532	N/A	-1.1983	N/A	Cytochrome P450	scaffold_9:940982-942847		
N	7	133728	N/A	-0.8147	N/A	-	scaffold_1:218104-219417		
N	7	172245	N/A	-0.4136	N/A	Unknown protein product	scaffold_1:276192-277028		
N	7	170369	N/A	-0.3795	N/A	-	scaffold_1:3134142-3139330		
N	7	196832	N/A	-0.5971	N/A	Hypothetical pseudouridylate synthase	scaffold_1:3330325-3331597		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	7	119505	N/A	-0.4639	N/A	-	scaffold_10:766187-769801		
N	7	136701	N/A	-0.8599	N/A	SAM-dependent methyltransferases	scaffold_11:1656398-1657240		
N	7	54282	N/A	-0.477	N/A	Hypothetical protein, contains RPR and RRM domains	scaffold_11:65898-68891		
N	7	122267	N/A	-0.5148	N/A	-	scaffold_11:661678-663427		
N	7	50299	N/A	-0.6931	N/A	Phosphatidylserine decarboxylase-related	scaffold_12:258035-259312		
N	7	44171	N/A	-0.5498	N/A	-	scaffold_13:581070-581570		
N	7	133888	N/A	-0.4132	N/A	Putative Zinc transporter ZIP, Zn /Fe	scaffold_14:468605-469991		
N	7	204165	N/A	-1.9551	N/A	Amino acid permease	scaffold_15:207290-209185		
N	7	54884	N/A	-0.4031	N/A	Shares amino acid sequence identity with the Saccharomyces cerevisiae MEF2 gene product comprising a mitochondrial elongation factor involved in translation.	scaffold_16:446978-449731		
N	7	37178	N/A	-0.5182	N/A	Serine/threonine protein kinase	scaffold_2:2419826-2421388		
N	7	197593	N/A	-0.5501	N/A	-	scaffold_2:2504272-2506240		
N	7	197132	N/A	-1.3537	N/A	-	scaffold_2:824253-825040		
N	7	45972	N/A	-1.3395	N/A	Hypothetical protein. Induced at pH 2.5.	scaffold_21:80530-82065		
N	7	52629	N/A	-0.5737	N/A	-	scaffold_3:1700262-1701994		
N	7	52532	N/A	-0.4507	N/A	-	scaffold_3:477901-478839		
N	7	142987	N/A	-0.346	N/A	N-6 Adenine-specific DNA methylase	scaffold_4:1315377-1315796		
N	7	208861	N/A	-2.2317	N/A	Hypothetical. Has Glucose-methanol-choline oxidoreductase and Glucose dehydrogenase/choline dehydrogenase/mandelonitrile lyase domains	scaffold_4:1487316-1488977		
N	7	48002	N/A	-0.4143	N/A	Amidohydrolase	scaffold_4:1551622-1552971		
N	7	39444	N/A	-0.3617	N/A	-	scaffold_4:2531875-2534691		
N	7	180870	N/A	-0.3485	N/A	Transferase	scaffold_5:155462-156907		
N	7	124658	N/A	-0.4535	N/A	-	scaffold_5:2169970-2171066		
N	7	182143	N/A	-0.3037	N/A	Cytochrome P450	scaffold_6:1048268-1050241		
N	7	209960	N/A	-0.2772	N/A	Porin, eukaryotic type	scaffold_6:78522-79737		
N	7	49546	N/A	-0.4368	N/A	-	scaffold_9:387331-389202		
N	8	51797	N/A	-0.8234	N/A	Predicted transcription factor	scaffold_1:1198454-1200810		
N	8	170454	N/A	-0.5114	N/A	Glycosyl transferase, group 1	scaffold_1:1284379-1285629		
N	8	36209	N/A	-0.445	N/A	-	scaffold_1:2890014-2892010		
N	8	205506	N/A	-0.3658	N/A	DNA-directed RNA polymerase II, largest subunit	scaffold_1:607713-613145		
N	8	46369	N/A	-0.3896	N/A	hypothetical protein with predicted SET domain and TPR repeat; KOG Class: Chromatin structure and dynamics; KOG Id: 2084; KOG Description: Predicted histone tail methylase containing SET domain	scaffold_1:793760-796136		
N	8	43416	N/A	-0.445	N/A	-	scaffold_11:1185235-1186051		
N	8	189135	N/A	-0.503	N/A	hypothetical carboxylesterase	scaffold_11:1200529-1202497		
N	8	43674	N/A	-0.5033	N/A	Ribonuclease II	scaffold_12:333037-336545		
N	8	43753	N/A	-0.4937	N/A	hypothetical protein with predicted C-5 cytosine-specific DNA methylase and a peptidase domain; Interpro Id: 1525; Interpro description:C-5 cytosine-specific DNA methylase; GO Desc.: DNA binding and DNA methylation	scaffold_12:575780-576817	125	
N	8	43754	N/A	-0.5653	N/A	-	scaffold_12:577834-578145	125	
N	8	54662	N/A	-0.3988	N/A	hypothetical SNF5/SMARCB1/INI1 protein - a key component of SWI/SNF-class complexes; KOG Class: Chromatin structure and dynamics; KOG Id: 1649; KOG Description: SWI-SNF chromatin remodeling complex, Snf5 subunit	scaffold_13:1142269-1144193		
N	8	213553	N/A	-0.4305	N/A	Anp1	scaffold_14:470643-471846		
N	8	213708	N/A	-0.4476	N/A	-	scaffold_15:184102-185914		
N	8	131636	N/A	-0.373	N/A	Fungal transcriptional regulatory protein	scaffold_15:594571-596584		
N	8	50908	N/A	-0.446	N/A	-	scaffold_15:662450-663290		
N	8	141462	N/A	-0.5958	N/A	-	scaffold_15:813869-815022		
N	8	213866	N/A	-0.6076	N/A	-	scaffold_16:123022-124680		
N	8	44977	N/A	-0.4707	N/A	-	scaffold_16:67823-70195		
N	8	134837	N/A	-0.4362	N/A	-	scaffold_16:801297-802127		
N	8	55058	N/A	-0.5557	N/A	Putative β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_18:167170-167909		
N	8	132816	N/A	-0.7925	N/A	-	scaffold_19:135673-137147		
N	8	132624	N/A	-0.3546	N/A	Fungal specific transcription factor	scaffold_3:1104166-1106047		
N	8	55789	N/A	-0.3327	N/A	-	scaffold_3:2222580-2224318		
N	8	176076	N/A	-0.593	N/A	Major facilitator superfamily	scaffold_3:2318973-2321015		
N	8	208318	N/A	-0.2524	N/A	3-phosphoglycerate kinase	scaffold_3:3093304-3094735		
N	8	177559	N/A	-0.3398	N/A	Related to dihydrolipoamide succinyltransferase (EC 2.3.1.61). May only be a subunit of the complex	scaffold_3:334920-336432		
N	8	208474	N/A	-0.3526	N/A	Phospholipid methyltransferase	scaffold_3:3499105-3500197		
N	8	39005	N/A	-0.5051	N/A	-	scaffold_4:1107518-1109069		
N	8	38756	N/A	-0.7638	N/A	-	scaffold_4:252407-253861		
N	8	179443	N/A	-0.3511	N/A	von Willebrand factor and related coagulation proteins	scaffold_4:565962-567847		
N	8	40244	N/A	-0.4802	N/A	oxidoreductase activity	scaffold_5:2307624-2308888		
N	8	40256	N/A	-0.311	N/A	Short-chain dehydrogenase/reductase	scaffold_5:2342671-2343591		
N	8	39650	N/A	-0.5964	N/A	-	scaffold_5:285554-286597		
N	8	141194	N/A	-0.5064	N/A	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 2510; KOG Description: SWI-SNF chromatin-remodeling complex protein	scaffold_6:225723-226943		
N	8	40929	N/A	-0.4127	N/A	Fungal transcriptional regulatory protein	scaffold_7:99371-101543		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	8	56583	N/A	-0.327	N/A	candidate UDP-glucose 4-epimerase	scaffold_8:978705-980046		
N	8	42214	N/A	-0.5422	N/A	Fungal transcriptional regulatory protein	scaffold_9:588674-590383		
N	9	205624	N/A	-0.5614	N/A	hypothetical. Histidine acid phosphatase	scaffold_1:1083949-1085903		
N	9	52020	N/A	-0.44	N/A	Ribosomal protein	scaffold_1:3091168-3092455		
N	9	196819	N/A	-0.6765	N/A	RNA polymerase	scaffold_1:3307377-3307905		
N	9	212180	N/A	-0.5563	N/A	Putative GroEL-like chaperone, ATPase	scaffold_10:1746106-1748217		
N	9	56836	N/A	-0.5846	N/A	rhoA, Ras-related small GTPase	scaffold_10:1826349-1827288		
N	9	50260	N/A	-0.4762	N/A	Hypothetical, contains SPRY domain	scaffold_12:22929-23864		
N	9	54440	N/A	-0.7502	N/A	Hypothetical protein with RRM domain	scaffold_12:46583-47442		
N	9	203496	N/A	-0.3399	N/A	Major facilitator superfamily	scaffold_13:285068-293740		
N	9	213563	N/A	-0.5998	N/A	Exosomal 3′-5′ exoribonuclease complex, subunit Rrp46	scaffold_14:493378-494220		
N	9	44518	N/A	-0.3284	N/A	related to extracellular tannase	scaffold_14:542166-543878		
N	9	52219	N/A	-1.193	N/A	Glycoside hydrolase, family 28	scaffold_2:1245766-1246999		
N	9	52249	N/A	-0.5127	N/A	Vesicle coat complex COPI, β' subunit	scaffold_2:1472793-1475744		
N	9	173689	N/A	-0.4113	N/A	Protein kinase	scaffold_2:2632558-2634732		
N	9	130186	N/A	-0.412	N/A	Aconitate hydratase, mitochondrial	scaffold_2:3115932-3118146		
N	9	129219	N/A	-0.3702	N/A	Glycoside hydrolase, family 18	scaffold_2:3671924-3675628		
N	9	207503	N/A	-0.4348	N/A	Ammonium Transporter Family	scaffold_2:3883793-3885642		
N	9	206469	N/A	-0.438	N/A	-	scaffold_2:400434-402674		
N	9	55517	N/A	-0.4363	N/A	Phenylalanyl-tRNA synthetase	scaffold_2:471038-472582		
N	9	195189	N/A	-0.3132	N/A	-	scaffold_22:49903-51328		
N	9	38292	N/A	-0.2684	N/A	-	scaffold_3:2206556-2207074		
N	9	38383	N/A	-0.5612	N/A	Small nuclear ribonucleoprotein	scaffold_3:2657191-2657573		
N	9	47596	N/A	-0.6886	N/A	-	scaffold_3:2740605-2741736		
N	9	198862	N/A	-0.4785	N/A	Ribosomal protein S11	scaffold_3:3228102-3228809		
N	9	47711	N/A	-0.393	N/A	G-protein β subunit-like protein (contains WD40 repeats)	scaffold_3:3365344-3366735		
N	9	129528	N/A	-0.5663	N/A	-	scaffold_3:3380257-3383732		
N	9	208493	N/A	-0.8338	N/A	-	scaffold_3:3530347-3533322		
N	9	47332	N/A	-0.4171	N/A	Ubiquitin-conjugating enzymes	scaffold_3:846696-847383		
N	9	178088	N/A	-0.3156	N/A	-	scaffold_4:1266901-1267659		
N	9	47986	N/A	-0.6188	N/A	hypothetical Peroxisomal biogenesis factor 11	scaffold_4:1443918-1444721		
N	9	209292	N/A	-0.4625	N/A	Hypothetical RING finger domain protein	scaffold_5:173092-175011		
N	9	179968	N/A	-0.2881	N/A	Squalene/phytoene synthase	scaffold_5:2279166-2281182		
N	9	210076	N/A	-0.2921	N/A	General substrate transporter	scaffold_6:514683-516299		
N	9	41339	N/A	-0.5783	N/A	-	scaffold_7:1461755-1464537		
N	9	139390	N/A	-0.4612	N/A	Fungal specific transcription factor	scaffold_7:1705122-1706678		
N	9	138447	N/A	-0.382	N/A	hypothetical protein with esterase/lipase/thioesterase and signal peptide motifs	scaffold_736:803-1200		
N	9	41626	N/A	-0.5284	N/A	Predicted membrane protein	scaffold_8:524143-527594		
N	9	53723	N/A	-0.6553	N/A	C4-dicarboxylate transporter/malic acid transport protein	scaffold_8:80584-81811		
N	10	35746	N/A	-0.5189	N/A	-	scaffold_1:1239951-1240256		
N	10	51862	N/A	-0.4217	N/A	Flavin reductase-like	scaffold_1:1653309-1653893		
N	10	55358	N/A	-0.4887	N/A	AIR carboxylase	scaffold_1:1706492-1708534		
N	10	36162	N/A	-0.9565	N/A	-	scaffold_1:2521506-2522805		
N	10	51987	N/A	-0.3557	N/A	(bimG) Serine/threonine-specific protein phosphatase (bimG). Deduced from identity to the A. nidulans gene	scaffold_1:2876773-2878077		
N	10	143973	N/A	-0.5981	N/A	-	scaffold_1:342939-343115		
N	10	171001	N/A	-0.4885	N/A	-	scaffold_1:851254-851907		
N	10	187784	N/A	-0.516	N/A	Hypothetical. Monocarboxylate transporter like	scaffold_10:1160548-1162119		
N	10	202700	N/A	-0.4091	N/A	Multifunctional chaperone (14-3-3 family)	scaffold_10:1881249-1882674		
N	10	202301	N/A	-0.5509	N/A	candidate transcription initiation factor IIF	scaffold_10:426120-427531		
N	10	42762	N/A	-0.3804	N/A	-	scaffold_10:617452-619705		
N	10	188511	N/A	-0.9196	N/A	-	scaffold_11:1023200-1023905		
N	10	56954	N/A	-0.5098	N/A	-	scaffold_11:1460260-1461267		
N	10	56903	N/A	-0.2944	N/A	Eukaryotic translation initiation factor	scaffold_11:421297-422512		
N	10	212481	N/A	-0.375	N/A	-	scaffold_11:450142-451320		
N	10	50350	N/A	-0.3877	N/A	hypothetical Fungal transcriptional regulatory protein, N-terminal	scaffold_12:645455-646654		
N	10	120585	N/A	-0.3124	N/A	Tyrosine protein kinase	scaffold_16:777668-780025		
N	10	127967	N/A	-0.5867	N/A	-	scaffold_17:460069-460654		
N	10	57369	N/A	-0.4012	N/A	Hypothetical component of the ubiquinol-cytochrome c reductase complex (complex III or cytochrome b-c1 complex), which is part of the mitochondrial respiratory chain that generates an electrochemical potential coupled to ATP synthesis; the complex couples electron transfer from ubiquinol to cytochrome c	scaffold_17:592980-593813		
N	10	206907	N/A	-0.3854	N/A	-	scaffold_2:1658710-1659455		
N	10	52315	N/A	-0.5647	N/A	-	scaffold_2:1932648-1934168		
N	10	207067	N/A	-1.0867	N/A	HAD-superfamily hydrolase,	scaffold_2:2352882-2354288		
N	10	37207	N/A	-0.928	N/A	Hypothetical Cation transport ATPase, Copper translocation	scaffold_2:2524963-2528739		
N	10	197851	N/A	-0.3026	N/A	Sucrose transporter and related proteins	scaffold_2:3351115-3353299		
N	10	175546	N/A	-0.4216	N/A	Major facilitator superfamily	scaffold_2:3507280-3508965		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	10	207465	N/A	-0.4846	N/A	RNA-binding protein (contains RRM and Pumilio-like repeats)	scaffold_2:3762106-3765786		
N	10	195271	N/A	-0.8958	N/A	SAM (and some other nucleotide) binding motif	scaffold_24:603-1557		
N	10	176968	N/A	-0.496	N/A	Cytochrome P450	scaffold_3:1558002-1559637		
N	10	175708	N/A	-0.2742	N/A	-	scaffold_3:2352295-2353230		
N	10	198063	N/A	-0.3675	N/A	(suc1) extracellular GH family 32 β-fructofuranosidase (invertase)	scaffold_3:265236-267005		
N	10	175679	N/A	-0.4348	N/A	Pre-mRNA splicing factor	scaffold_3:2945701-2947062		
N	10	208390	N/A	-0.7186	N/A	Ankyrin repeat	scaffold_3:3268303-3268959		
N	10	35358	N/A	-0.4223	N/A	CCAAT-binding transcription factor,	scaffold_335:614-1465		
N	10	39181	N/A	-0.4902	N/A	Serine carboxypeptidases	scaffold_4:1654778-1656451		
N	10	52998	N/A	-0.4601	N/A	Hypothetical protein. Pfam suggests activity similar to the SAM-dependent methyltransferase/cell division protein FtsJ	scaffold_4:1717758-1719056		
N	10	138207	N/A	-0.4896	N/A	Mitochondrial Chaperonin Cpn10	scaffold_4:194045-194443		
N	10	39426	N/A	-0.5151	N/A	sn-1,2-diacylglycerol ethanolamine- and cholinephosphotranferases	scaffold_4:2478045-2479667		
N	10	47875	N/A	-0.5641	N/A	Flavonol reductase/cinnamoyl-CoA reductase	scaffold_4:692093-693055		
N	10	181535	N/A	-0.4659	N/A	-	scaffold_5:1942579-1943598		
N	10	142342	N/A	-0.4039	N/A	Iron/ascorbate family oxidoreductases	scaffold_5:2265784-2266779		
N	10	40660	N/A	-0.3211	N/A	Heterokaryon incompatibility factor	scaffold_6:1251298-1253772		
N	10	181975	N/A	-0.7912	N/A	Hypothetical Alkaline phytoceramidase	scaffold_6:1319938-1321160		
N	10	182423	N/A	-0.3554	N/A	Major facilitator superfamily	scaffold_6:1504864-1506731		
N	10	210387	N/A	-0.5206	N/A	(pelF) Pectine lyase F. Involved in pectine degradation (EC 4.2.2.10)	scaffold_6:1817701-1819245		
N	10	143395	N/A	-0.403	N/A	-	scaffold_6:1853740-1854243		
N	10	41393	N/A	-0.7388	N/A	-	scaffold_7:1619941-1620549		
N	10	141662	N/A	-0.5281	N/A	-	scaffold_7:1647434-1648122		
N	10	210431	N/A	-0.4772	N/A	-	scaffold_7:241711-242373		
N	10	41496	N/A	-0.3875	N/A	-	scaffold_8:136024-138401		
N	10	201544	N/A	-0.6948	N/A	-	scaffold_8:786253-787307		
N	10	185000	N/A	-0.8388	N/A	Cytochrome P450	scaffold_8:982385-984111		
N	10	186309	N/A	-0.4676	N/A	-	scaffold_9:122261-123887		
N	11	196559	N/A	-0.5572	N/A	-	scaffold_1:2394979-2396721		
N	11	36142	N/A	-0.4666	N/A	-	scaffold_1:2442757-2445230		
N	11	42654	N/A	-0.5899	N/A	hypothetical protein containing Zn-finger and Homeobox domains	scaffold_10:276681-278282		
N	11	137779	N/A	-0.5383	N/A	-	scaffold_10:629089-629382		
N	11	143018	N/A	-0.5429	N/A	Predicted short chain-type dehydrogenase	scaffold_12:1118375-1119341		
N	11	50281	N/A	-0.5736	N/A	-	scaffold_12:149762-150624		
N	11	189676	N/A	-0.4146	N/A	Malate/L-lactate dehydrogenase	scaffold_12:976768-977835		
N	11	191077	N/A	-0.5309	N/A	-	scaffold_13:553485-555353		
N	11	44249	N/A	-0.3569	N/A	-	scaffold_13:816450-818544		
N	11	203739	N/A	-0.411	N/A	Hypothetical ubiquinol cytochrome c reductase, subunit QCR7	scaffold_13:911021-911894		
N	11	191838	N/A	-0.5145	N/A	GPR1/FUN34 family protein	scaffold_15:511027-512005		
N	11	137941	N/A	-0.7245	N/A	-	scaffold_17:680860-681686		
N	11	37300	N/A	-0.5935	N/A	-	scaffold_2:2885115-2886223		
N	11	175167	N/A	-0.4431	N/A	hypothetical Silent Information regulator protein Sir2p; KOG Class: Chromatin structure and dynamics; KOG Id: 2682; KOG Description:NAD-dependent histone deacetylases and class I sirtuins (SIR2 family)	scaffold_2:3878384-3879632		
N	11	127627	N/A	-0.3518	N/A	Candidate ribosomal protein S18	scaffold_2:3929801-3930586		
N	11	119224	N/A	-0.6399	N/A	Transcription coactivator	scaffold_3:2080142-2083489		
N	11	207707	N/A	-0.3016	N/A	Hypothetical NADH:ubiquinone oxidoreductase, NDUFA9/39kDa subunit	scaffold_3:741996-743569		
N	11	179383	N/A	-0.4454	N/A	-	scaffold_4:1981047-1982513		
N	11	124451	N/A	-0.5256	N/A	Esterase/lipase/thioesterase	scaffold_5:1405945-1407126		
N	11	200174	N/A	-0.3507	N/A	von Willebrand factor and related coagulation proteins	scaffold_5:1503077-1504127		
N	11	209349	N/A	-0.4766	N/A	-	scaffold_5:317337-318024		
N	11	181503	N/A	-0.4929	N/A	Fungal specific transcription factor	scaffold_5:651004-653500		
N	11	180112	N/A	-0.2728	N/A	Predicted methyltransferase	scaffold_5:870494-871602		
N	11	39593	N/A	-0.7524	N/A	Hypothetical V-SNARE	scaffold_5:95389-96109		
N	11	40379	N/A	-0.6587	N/A	-	scaffold_6:285808-287425		
N	11	56436	N/A	-0.4706	N/A	-	scaffold_7:591626-593618		
N	11	49039	N/A	-0.3988	N/A	Hypothetical protein containing Sec23/Sec24 domains involved in vesicle coating	scaffold_7:734074-737363		
N	11	184433	N/A	-0.3804	N/A	contains SNF2 family DNA-dependent ATPase domain)	scaffold_8:297747-301446		
N	11	56582	N/A	-0.3918	N/A	-	scaffold_8:956686-959243		
N	11	130344	N/A	-0.4485	N/A	Fungal specific transcription factor	scaffold_9:1407548-1409960		
N	12	187401	N/A	-0.4494	N/A	Endoplasmic reticulum protein EP58	scaffold_10:1062449-1066754		
N	12	212147	N/A	-0.6731	N/A	Hypothetical. Related to major facilitator superfamily/Synaptic vesicle transporter SVOP	scaffold_10:1255083-1256972		
N	12	187479	N/A	-0.6735	N/A	vacuolar membrane PQ loop protein	scaffold_10:1772916-1774126		
N	12	188037	N/A	-0.6573	N/A	Lipoate-protein ligase A	scaffold_10:1811955-1813454		
N	12	54156	N/A	-0.3555	N/A	putative Heat shock protein DnaJ	scaffold_10:842896-844663		
N	12	54168	N/A	-0.4959	N/A	-	scaffold_10:946612-948216		
N	12	129379	N/A	-1.7279	N/A	-	scaffold_13:1076661-1080071		
N	12	54922	N/A	-0.6627	N/A	Putative α-1,2-mannosyltransferase	scaffold_16:746051-747994		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	12	173972	N/A	-0.4148	N/A	Flavonol reductase/cinnamoyl-CoA reductase	scaffold_2:2850156-2851256		
N	12	206674	N/A	-0.4938	N/A	Peptidase S16, lon protease	scaffold_2:969014-972410		
N	12	47573	N/A	-0.4418	N/A	processing peptidase	scaffold_3:2622006-2623844		
N	12	48908	N/A	-0.5176	N/A	Fatty acid desaturase	scaffold_7:72065-73739		
N	12	201516	N/A	-0.5542	N/A	-	scaffold_8:668347-669126		
N	12	211700	N/A	-0.3864	N/A	-	scaffold_9:1547579-1554840		
N	12	42356	N/A	-0.3279	N/A	Protein-kinase like	scaffold_9:990074-991467		
N	13	35983	N/A	-0.3999	N/A	Conserved hypothetical ATP binding protein	scaffold_1:1947346-1948600		
N	13	55395	N/A	-0.44	N/A	-	scaffold_1:2167397-2170102		
N	13	172049	N/A	-0.3188	N/A	Hypothetical NAD-dependent glycerol-3-phosphate dehydrogenase	scaffold_1:2176251-2177643		
N	13	52004	N/A	-0.3321	N/A	oxidoreductase	scaffold_1:2975083-2980464		
N	13	206214	N/A	-0.5561	N/A	NifU-like domain-containing proteins	scaffold_1:3016026-3017167		
N	13	171241	N/A	-0.5595	N/A	Splicing coactivator SRm160	scaffold_1:455873-461023		
N	13	186978	N/A	-0.3027	N/A	-	scaffold_10:1775009-1777222		
N	13	187743	N/A	-0.2755	N/A	-	scaffold_10:1814098-1816810		
N	13	43042	N/A	-0.6452	N/A	-	scaffold_10:1956686-1958953		
N	13	56853	N/A	-0.5266	N/A	Deduced translation product shares amino acid sequence identity with the Saccharomyces cerevisiae PNO1 gene product; an essential nucleolar protein required for pre-18S rRNA processing; in yeast Pno1p interacts with Dim1p, an 18S rRNA dimethyltransferase, and also with Nob1p, which is involved in proteasome biogenesis; contains a KH domain.	scaffold_10:1967970-1968879		
N	13	54391	N/A	-0.5129	N/A	Hypothetical homoserine O-acetyltransferase (EC 2.3.1.31).	scaffold_11:1087078-1088457		
N	13	56950	N/A	-0.5194	N/A	Candidate Lysophospholipase precursor (Phospholipase B)	scaffold_11:1436585-1438842		
N	13	43123	N/A	-0.5194	N/A	Ferredoxin	scaffold_11:214985-215725		
N	13	50014	N/A	-0.4173	N/A	RNA polymerase III (C) subunit	scaffold_11:80111-82241		
N	13	43691	N/A	-0.6671	N/A	Cytochrome P450	scaffold_12:385098-387012		
N	13	120896	N/A	-0.4351	N/A	Fungal specific transcription factor	scaffold_12:564114-566269		
N	13	143858	N/A	-0.4042	N/A	-	scaffold_13:1180688-1181229		
N	13	44126	N/A	-0.434	N/A	Nucleolar GTPase/ATPase p130	scaffold_13:471485-472230		
N	13	190860	N/A	-0.5671	N/A	Threonine dehydratase	scaffold_13:538181-539999		
N	13	203604	N/A	-0.4532	N/A	Aminoacyl-tRNA synthetase	scaffold_13:609202-611340		
N	13	203692	N/A	-0.3257	N/A	Hypothetical diphosphomevalonate decarboxylase	scaffold_13:812308-813588		
N	13	213531	N/A	-0.3496	N/A	Mitochondrial import translocase, subunit Tom70	scaffold_14:406952-409096		
N	13	44596	N/A	-0.7888	N/A	GCN5-related N-acetyltransferase	scaffold_14:808681-809493		
N	13	44741	N/A	-0.7716	N/A	-	scaffold_15:270622-273243		
N	13	57277	N/A	-0.3716	N/A	yop1 (A. fumigatus), Protein involved in membrane traffic (YOP1/TB2/DP1/HVA22 family)	scaffold_16:655577-656708		
N	13	54939	N/A	-0.6699	N/A	Amino acid/polyamine transporter	scaffold_16:873107-875146		
N	13	214651	N/A	-0.6374	N/A	Mannitol dehydrogenase	scaffold_19:147752-149260		
N	13	131028	N/A	-0.351	N/A	Geranylgeranyl pyrophosphate synthase/	scaffold_19:212893-214901		
N	13	194532	N/A	-0.4508	N/A	-	scaffold_19:27116-29908		
N	13	45764	N/A	-0.6883	N/A	hypothetical aspartate transaminase (EC 2.6.1.1)	scaffold_19:387365-388870		
N	13	173794	N/A	-0.472	N/A	-	scaffold_2:1026192-1026777		
N	13	173647	N/A	-0.5257	N/A	Zn-finger, C-x8-C-x5-C-x3-H type	scaffold_2:1432254-1434731		
N	13	206911	N/A	-0.335	N/A	Hypothetical protein tyrosine phosphatase	scaffold_2:1660671-1662145		
N	13	37152	N/A	-0.5187	N/A	related to short-chain alcohol dehydrogenases)	scaffold_2:2050679-2051779		
N	13	37328	N/A	-0.9279	N/A	-	scaffold_2:2988529-2989826		
N	13	207313	N/A	-0.5501	N/A	transmembrane protein	scaffold_2:3276923-3278714		
N	13	207418	N/A	-1.4041	N/A	phospholipid catabolism	scaffold_2:3576074-3578092		
N	13	37541	N/A	-0.5397	N/A	phosphopantothenoylcysteine synthetase/decarboxylase	scaffold_2:3655730-3657012		
N	13	55534	N/A	-0.6756	N/A	-	scaffold_2:765364-766369		
N	13	174653	N/A	-0.4182	N/A	-	scaffold_2:979982-980802		
N	13	198287	N/A	-0.4063	N/A	Ubiquitin-like protein	scaffold_3:1160176-1161639		
N	13	198312	N/A	-0.6267	N/A	Reticulon-like protein	scaffold_3:1268908-1270277		
N	13	125153	N/A	-0.382	N/A	-	scaffold_3:2017098-2018321		
N	13	208093	N/A	-0.4538	N/A	-	scaffold_3:2264818-2266321	126	
N	13	52698	N/A	-0.721	N/A	-	scaffold_3:2269514-2270367	126	
N	13	208165	N/A	-0.4121	N/A	Serine palmitoyltransferase	scaffold_3:2615421-2617157		
N	13	208225	N/A	-0.4962	N/A	putative ATP dependent clp protease	scaffold_3:2791087-2793483		
N	13	177976	N/A	-0.3902	N/A	-	scaffold_3:3371110-3371838		
N	13	177060	N/A	-0.6043	N/A	Permease of the drug/metabolite transporter (DMT) superfamily	scaffold_3:3427726-3429011		
N	13	207677	N/A	-0.4785	N/A	Deduced amino acid sequence shares identity with the Saccharomyces cerevisiae MRP49 gene product; a mitochondrial ribosomal protein of the large subunit.	scaffold_3:697314-698157		
N	13	38978	N/A	-0.3549	N/A	Flavoprotein monooxygenase	scaffold_4:1024245-1025532		
N	13	178093	N/A	-0.572	N/A	Nicotinamide mononucleotide adenylyl transferase	scaffold_4:1703288-1704285		
N	13	119446	N/A	-0.4925	N/A	Hypothetical trehalose-phosphatase	scaffold_4:2836057-2839021		
N	13	208651	N/A	-0.3713	N/A	Mitochondrial import inner membrane translocase subunit Tim7	scaffold_4:570097-570833		
N	13	208695	N/A	-0.4384	N/A	Aminotransferase	scaffold_4:735561-737106		
N	13	39912	N/A	-0.6554	N/A	DMQ mono-oxygenase	scaffold_5:1185549-1186313		
N	13	56120	N/A	-0.4573	N/A	Nucleolar GTPase/ATPase p130	scaffold_5:130109-131677		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	13	181348	N/A	-0.6405	N/A	Predicted PRP38-like splicing factor	scaffold_5:1527059-1527823		
N	13	53301	N/A	-0.5525	N/A	-	scaffold_5:1615212-1615804		
N	13	40050	N/A	-0.4553	N/A	hypothetical WW/Rsp5/WWP; KOG Class: Chromatin structure and dynamics	scaffold_5:1674870-1675739		
N	13	40260	N/A	-0.399	N/A	Major facilitator superfamily	scaffold_5:2352396-2353752		
N	13	53175	N/A	-0.9098	N/A	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_5:435253-437525		
N	13	199912	N/A	-0.4613	N/A	Oxysterol-binding protein	scaffold_5:557264-559075		
N	13	128105	N/A	-0.782	N/A	-	scaffold_6:130370-130759		
N	13	210274	N/A	-0.4709	N/A	NADP-dependent flavoprotein reductase	scaffold_6:1453572-1458168		
N	13	210350	N/A	-0.3414	N/A	Major facilitator superfamily	scaffold_6:1710311-1712159		
N	13	183278	N/A	-0.5814	N/A	Related to tryptophan synthase. Shows similarity to N. crassa tryptophan synthase of N. crassa	scaffold_7:911756-913967		
N	13	49455	N/A	-0.4024	N/A	-	scaffold_8:1569160-1570743		
N	13	53706	N/A	-0.673	N/A	Related to C-4 methylsterol monooxygenase	scaffold_8:1618-2678		
N	13	41991	N/A	-0.5973	N/A	Mitochondrial substrate carrier	scaffold_8:1641507-1642752		
N	13	210968	N/A	-0.4548	N/A	Predicted RNA-binding protein (RRM superfamily)	scaffold_8:414017-415122		
N	13	185870	N/A	-0.5408	N/A	No homology to confirmed arginine N-methyltransferases (EC 2.1.1.2)	scaffold_9:1093539-1094795		
N	13	53945	N/A	-1.2561	N/A	Haem peroxidase, plant/fungal/bacterial	scaffold_9:268420-270698		
N	13	128935	N/A	-0.3612	N/A	Major facilitator superfamily	scaffold_9:313980-319031		
N	14	118832	N/A	-0.7406	N/A	ABC transporter	scaffold_1:1243820-1248328		
N	14	124202	N/A	-0.5278	N/A	tRNA(1-methyladenosine) methyltransferase, subunit GCD14	scaffold_1:1676533-1677852		
N	14	171679	N/A	-0.4193	N/A	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae RET1 gene product; the second-largest subunit of RNA polymerase III, which is responsible for the transcription of tRNA and 5S RNA genes, and other low molecular weight RNAs.	scaffold_1:2251868-2255672		
N	14	51711	N/A	-0.4102	N/A	adB. Almost identical to E. nidulans adenylosuccinate synthase (adB) (EC 6.3.4.4)	scaffold_1:278915-280425		
N	14	172399	N/A	-0.3497	N/A	-	scaffold_1:3048552-3049019		
N	14	55468	N/A	-0.563	N/A	-	scaffold_1:3106469-3106951		
N	14	122683	N/A	-0.4593	N/A	-	scaffold_1:819391-820881		
N	14	205603	N/A	-0.892	N/A	hypothetical. Choline kinase	scaffold_1:990921-993355		
N	14	127671	N/A	-0.3136	N/A	-	scaffold_10:484759-485151		
N	14	50403	N/A	-1.0157	N/A	Kinesin-like protein	scaffold_12:1132042-1133385		
N	14	213343	N/A	-0.8696	N/A	Predicted 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase	scaffold_13:1085361-1088652		
N	14	44179	N/A	-0.4799	N/A	Nuclear transport factor 2	scaffold_13:608335-608882		
N	14	140582	N/A	-0.3048	N/A	Zn-finger, C-x8-C-x5-C-x3-H type	scaffold_15:584478-585900		
N	14	126043	N/A	-0.4244	N/A	-	scaffold_16:12247-12849		
N	14	133271	N/A	-0.5675	N/A	-	scaffold_17:439042-440935		
N	14	120572	N/A	-0.534	N/A	N-methyltransferase	scaffold_17:477266-479393		
N	14	129315	N/A	-0.5771	N/A	Protein kinase	scaffold_18:279374-284144		
N	14	36623	N/A	-0.8689	N/A	-	scaffold_2:178643-179453		
N	14	207011	N/A	-0.6176	N/A	Oxysterol-binding protein	scaffold_2:1903351-1904817		
N	14	37131	N/A	-0.6292	N/A	Fungal specific transcription factor	scaffold_2:1983775-1987116		
N	14	37245	N/A	-0.7162	N/A	Hypothetical protein.	scaffold_2:2665733-2667559		
N	14	207328	N/A	-0.5059	N/A	Peptidase	scaffold_2:3313938-3314875		
N	14	55539	N/A	-0.4671	N/A	Methylenetetrahydrofolate reductase	scaffold_2:860468-862471		
N	14	45871	N/A	-0.4833	N/A	-	scaffold_20:114289-115424		
N	14	176840	N/A	-0.6237	N/A	Predicted exosome subunit	scaffold_3:1232230-1233422		
N	14	176254	N/A	-0.6239	N/A	-	scaffold_3:1550291-1550827		
N	14	47218	N/A	-0.5381	N/A	-	scaffold_3:184077-184778		
N	14	47594	N/A	-0.6839	N/A	-	scaffold_3:2731989-2733141		
N	14	129162	N/A	-0.4087	N/A	-	scaffold_4:1255806-1259933		
N	14	52962	N/A	-0.7102	N/A	Hypothetical pyridoxal-dependent decarboxylase. HMMPfam indicates this activity. No homology to confirmed pyridoxal-dependent decarboxylases was found	scaffold_4:1283560-1285074		
N	14	124912	N/A	-0.8658	N/A	Choline kinase	scaffold_4:1579658-1580743		
N	14	39275	N/A	-0.5903	N/A	Predicted ATPase, nucleotide-binding	scaffold_4:1987226-1988385		
N	14	48140	N/A	-0.3111	N/A	Fungal transcriptional regulatory protein, N-terminal	scaffold_4:2581678-2584189		
N	14	199601	N/A	-0.384	N/A	-	scaffold_4:2655776-2659943		
N	14	209193	N/A	-0.5037	N/A	-	scaffold_4:2897991-2898575		
N	14	47869	N/A	-0.4892	N/A	-	scaffold_4:664566-667410		
N	14	55967	N/A	-0.8349	N/A	Cytochrome P450	scaffold_4:887770-889601		
N	14	56196	N/A	-0.2842	N/A	related to Candida albicans aspartyl-tRNA synthase	scaffold_5:1097930-1099667		
N	14	180846	N/A	-0.6749	N/A	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_5:1520704-1521937		
N	14	129576	N/A	-0.53	N/A	-	scaffold_5:1610707-1613921		
N	14	209775	N/A	-0.7738	N/A	-	scaffold_5:1741580-1742686		
N	14	180930	N/A	-0.6244	N/A	-	scaffold_5:1932578-1934227		
N	14	40339	N/A	-0.7931	N/A	Armadillo/beta-catenin-like repeat-containing protein	scaffold_6:171233-171968		
N	14	40937	N/A	-0.4816	N/A	Hypothetical phosphoglycerate mutase; EC 5.4.2.1	scaffold_7:130414-131286		
N	14	41928	N/A	-0.5911	N/A	-	scaffold_8:1435333-1436358		
N	14	126717	N/A	-0.7458	N/A	hypothetical cell wall biosynthesis protein	scaffold_9:1625073-1626082		
N	14	49526	N/A	-0.9045	N/A	-	scaffold_9:271920-272683		
N	14	49539	N/A	-0.6206	N/A	Candidate nimA	scaffold_9:362814-365021		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	15	46421	N/A	-0.513	N/A	-	scaffold_1:1111958-1113084		
N	15	170651	N/A	-0.6533	N/A	-	scaffold_1:1776675-1777485		
N	15	46557	N/A	-0.3841	N/A	Myb, DNA-binding	scaffold_1:1858857-1860489		
N	15	196377	N/A	-0.4264	N/A	Mitochondrial/chloroplast ribosomal protein L2	scaffold_1:1866656-1867952		
N	15	36183	N/A	-0.6439	N/A	Hypothetical RNA polymerase subunit	scaffold_1:2761582-2762335		
N	15	131964	N/A	-0.4528	N/A	GTP1/OBG subdomain	scaffold_1:310695-312224		
N	15	51724	N/A	-0.7424	N/A	Hypothetical Molecular chaperone Prefoldin	scaffold_1:426725-427437		
N	15	54270	N/A	-0.421	N/A	Predicted translation initiation factor related to eIF-2B $\alpha/\beta/\delta$ subunits (CIG2/IDI2)	scaffold_10:2002867-2004067		
N	15	211951	N/A	-0.3207	N/A	Phenylalanyl-tRNA synthetase, β subunit archae/euk cytosolic	scaffold_10:756270-758530		
N	15	189070	N/A	-0.4098	N/A	snoRNP protein NOP10.	scaffold_11:245107-245388		
N	15	56891	N/A	-0.3436	N/A	Shares amino acid sequence identity to Saccharomyces cerevisiae GUS1 gene product comprising a glutamyl-tRNA synthetase (GluRS); forms a complex with methionyl-tRNA synthetase (Mes1p) and Arc1p; complex formation increases the catalytic efficiency of both tRNA synthetases and ensures their correct localization to the cytoplasm.	scaffold_11:287401-289595		
N	15	212557	N/A	-0.3545	N/A	Sec1-like protein	scaffold_11:754806-757111		
N	15	189935	N/A	-0.4499	N/A	RNA polymerase N/8 Kd subunit. DNA-dependent RNA polymerase catalyzes the transcription of DNA into RNA using the four ribonucleoside triphosphates as substrates	scaffold_12:4763-5158		
N	15	144231	N/A	-0.6901	N/A	-	scaffold_13:1106516-1106686		
N	15	190873	N/A	-0.8065	N/A	GCN5-related N-acetyltransferase	scaffold_13:524810-525325		
N	15	190259	N/A	-0.5189	N/A	-	scaffold_13:781105-781982		
N	15	44393	N/A	-0.4976	N/A	-	scaffold_14:113205-113780		
N	15	57187	N/A	-0.6364	N/A	Cytochrome P450	scaffold_15:30841-32602		
N	15	50995	N/A	-0.5302	N/A	Hypothetical. G-protein. WD40 repeat-containing	scaffold_16:369157-370935		
N	15	192770	N/A	-0.3805	N/A	hypothetical protein with predicted NAP and Poly(A) polymerase domains; KOG Class: Chromatin structure and dynamics; KOG Id: 1507; KOG Description: Nucleosome assembly protein NAP-1	scaffold_16:898471-899956	127	
N	15	214148	N/A	-0.781	N/A	Cation transport ATPase	scaffold_16:901292-906165	127	
N	15	132036	N/A	-0.6089	N/A	-	scaffold_17:304206-306232		
N	15	194066	N/A	-0.3999	N/A	-	scaffold_18:22803-24032		
N	15	125918	N/A	-0.6412	N/A	RNA-binding proteins	scaffold_18:449217-450190		
N	15	214561	N/A	-0.4814	N/A	Methylenetetrahydrofolate dehydrogenase/methylenetetrahydrofolate cyclohydrolase	scaffold_18:469956-471261		
N	15	52208	N/A	-0.6253	N/A	-	scaffold_2:1132942-1133950		
N	15	36895	N/A	-0.5152	N/A	SAM-dependent methyltransferases	scaffold_2:1169839-1171584		
N	15	197261	N/A	-0.4907	N/A	Arginyl-tRNA synthetase	scaffold_2:1239833-1241967		
N	15	47000	N/A	-0.4078	N/A	-	scaffold_2:1530375-1531775		
N	15	175249	N/A	-0.6059	N/A	Dynactin	scaffold_2:1583358-1585451		
N	15	52291	N/A	-0.4451	N/A	Anion-transporting ATPase	scaffold_2:1790401-1791449		
N	15	136694	N/A	-0.6529	N/A	Translin family protein	scaffold_2:2068974-2070164		
N	15	52335	N/A	-0.5142	N/A	Related to protein arginine N-methyltransferase (E. nidulans)	scaffold_2:2430375-2432273		
N	15	47076	N/A	-0.3055	N/A	Uncharacterized conserved protein	scaffold_2:2586527-2587123		
N	15	37382	N/A	-0.6015	N/A	Mitochondrial/chloroplast ribosomal protein L54/L37	scaffold_2:3163775-3164573		
N	15	207470	N/A	-0.3244	N/A	Hypothetical cytosolic asparaginyl-tRNA synthetase	scaffold_2:3791226-3793030		
N	15	206525	N/A	-0.403	N/A	Tyrosyl-tRNA synthetase,	scaffold_2:526298-527773		
N	15	120353	N/A	-0.4099	N/A	Hypothetical protein with PPR repeat	scaffold_2:683475-685476		
N	15	36779	N/A	-0.3168	N/A	Hypothetical dihydroorotate dehydrogenase (EC 1.3.3.1)	scaffold_2:757134-758772		
N	15	198321	N/A	-0.388	N/A	Aldehyde dehydrogenase	scaffold_3:1299674-1301185		
N	15	52713	N/A	-0.5479	N/A	Glucosamine 6-phosphate synthetases, contain amidotransferase and phosphosugar isomerase domains	scaffold_3:2572928-2574290		
N	15	122329	N/A	-0.4928	N/A	Fungal transcriptional regulatory protein, N-terminal	scaffold_3:2954257-2955836		
N	15	55991	N/A	-0.5855	N/A	papA, Prolyl aminopeptidase papA (EC 3.4.11.5)	scaffold_4:1285718-1287538		
N	15	53002	N/A	-0.5591	N/A	-	scaffold_4:1738949-1739928		
N	15	39312	N/A	-0.548	N/A	Thioredoxin-related	scaffold_4:2115852-2116400		
N	15	52878	N/A	-0.3579	N/A	Nuclear polyadenylated RNA binding protein	scaffold_4:418906-420454		
N	15	47847	N/A	-0.5892	N/A	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae POL5 gene product; a protein with sequence similarity to the human MybBP1A and weak sequence similar to B-type DNA polymerases, not required for chromosomal DNA replication; required for the synthesis of rRNA.	scaffold_4:508915-512084		
N	15	48500	N/A	-0.6137	N/A	-	scaffold_5:1797924-1799310		
N	15	40199	N/A	-0.4487	N/A	Sucrose transporter and related proteins	scaffold_5:2189116-2190825	128	
N	15	180990	N/A	-0.4858	N/A	Zinc-binding oxidoreductase	scaffold_5:2195688-2196957	128	
N	15	39788	N/A	-0.5148	N/A	Permease for cytosine/purines, uracil, thiamine, allantoin	scaffold_5:799403-801269		
N	15	48373	N/A	-0.7112	N/A	Uncharacterized conserved protein similar to ATP/GTP-binding protein	scaffold_5:954726-957395		
N	15	40771	N/A	-0.5243	N/A	Putative GroEL-like chaperone, ATPase	scaffold_6:1600232-1602240		
N	15	56267	N/A	-0.4195	N/A	-	scaffold_6:41513-42717		
N	15	40438	N/A	-0.3861	N/A	-	scaffold_6:572705-573733		
N	15	48704	N/A	-0.6005	N/A	-	scaffold_6:736779-738726		
N	15	210168	N/A	-0.6496	N/A	Transcription factor of the Forkhead/HNF3 family	scaffold_6:858790-860069		
N	15	56606	N/A	-0.8045	N/A	Mitochondrial/chloroplast ribosomal protein	scaffold_8:1206501-1207039		
N	15	211236	N/A	-0.4467	N/A	Cysteinyl-tRNA synthetase	scaffold_8:1262908-1265374		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	15	186794	N/A	-0.4007	N/A	Related to pseudouridine synthase.	scaffold_9:1342197-1343954		
N	16	35758	N/A	-0.6853	N/A	DEAD/DEAH box helicase	scaffold_1:1265317-1267902		
N	16	171099	N/A	-0.5802	N/A	snRNP-associated RNA splicing factor	scaffold_1:1277067-1278210		
N	16	171258	N/A	-0.7387	N/A	Predicted Protein prenyltransferase, α subunit	scaffold_1:1853347-1854969		
N	16	46686	N/A	-0.5032	N/A	prpA, pdiA related protein A	scaffold_1:2534464-2535984		
N	16	186946	N/A	-0.3435	N/A	Hypothetical protein. Putative Adenosine deaminase/editase	scaffold_10:793870-795497		
N	16	43941	N/A	-0.4258	N/A	Haloacid dehalogenase/epoxide hydrolase	scaffold_12:1135565-1136278		
N	16	54443	N/A	-0.348	N/A	-	scaffold_12:70694-71292		
N	16	190695	N/A	-0.5154	N/A	-	scaffold_13:1069073-1069754		
N	16	190658	N/A	-0.3512	N/A	hypothetical protein kinase	scaffold_13:928313-932803		
N	16	45120	N/A	-0.5724	N/A	Hypothetical protein with Zn-finger, C-x8-C-x5-C-x3-H type and an RRM domain	scaffold_16:519070-520296		
N	16	143320	N/A	-0.6387	N/A	Hypothetical inosine triphosphate pyrophosphatase	scaffold_16:891037-891833		
N	16	37320	N/A	-0.3114	N/A	Shares amino acid sequence identity to Saccharomyces cerevisiae FAL1 encoding a nucleolar protein required for maturation of 18S rRNA; member of the eIF4A subfamily of DEAD-box ATP-dependent RNA helicases.	scaffold_2:2964440-2965810		
N	16	138217	N/A	-0.6033	N/A	Predicted RNA-binding protein (RRM superfamily)	scaffold_2:3866852-3867625		
N	16	194911	N/A	-0.7029	N/A	Predicted NUDIX hydrolase FGF-2 and related proteins	scaffold_21:255458-256127		
N	16	38025	N/A	-0.3752	N/A	-	scaffold_3:1181509-1182656		
N	16	38216	N/A	-0.7222	N/A	Adenosine/AMP deaminase	scaffold_3:1961583-1962753		
N	16	198624	N/A	-0.4348	N/A	Ribosomal protein S6	scaffold_3:2385035-2385573	129	
N	16	38348	N/A	-0.5081	N/A	Acyl-CoA thioesterase	scaffold_3:2386460-2387575	129	
N	16	122545	N/A	-0.4503	N/A	Ubiquitin-conjugating enzymes	scaffold_3:2779759-2781138		
N	16	47604	N/A	-0.4256	N/A	-	scaffold_3:2788453-2789013		
N	16	38616	N/A	-0.7923	N/A	Transcriptional coactivator CAPER (RRM superfamily)	scaffold_3:3415227-3416251		
N	16	176332	N/A	-0.7763	N/A	-	scaffold_3:3581183-3581536		
N	16	39117	N/A	-0.6385	N/A	Hypothetical subunit of transcription initiation factor TFIID	scaffold_4:1462214-1465719		
N	16	38734	N/A	-0.5146	N/A	Polyadenylation factor I complex	scaffold_4:195145-196224		
N	16	178160	N/A	-0.8126	N/A	-	scaffold_4:2063758-2065033		
N	16	179474	N/A	-0.3724	N/A	Hypothetical RNA lariat debranching enzyme	scaffold_4:264789-267064		
N	16	38811	N/A	-0.3734	N/A	Sphingomyelinase family protein	scaffold_4:435327-436760	130	
N	16	122220	N/A	-0.3193	N/A	WD40 repeat-containing protein	scaffold_4:437148-438846	130	
N	16	209628	N/A	-1.4788	N/A	Hypothetical methyltransferase	scaffold_5:1206635-1207627		
N	16	40113	N/A	-0.2863	N/A	-	scaffold_5:1915004-1915876		
N	16	181005	N/A	-0.5039	N/A	-	scaffold_5:1951014-1951884		
N	16	48549	N/A	-0.3533	N/A	-	scaffold_5:2255728-2256888		
N	16	39748	N/A	-0.4833	N/A	-	scaffold_5:661964-663631		
N	16	183031	N/A	-0.5577	N/A	Hypothetical small nuclear ribonucleoprotein (snRNP)	scaffold_6:1433935-1434433		
N	16	40557	N/A	-0.5005	N/A	hypothetical protein with predicted bromodomain transcription factor and histone-fold	scaffold_6:927151-927798		
N	16	41315	N/A	-0.3484	N/A	Hypothetical Protein involved in inorganic phosphate transport	scaffold_7:1396219-1396944		
N	16	40972	N/A	-0.3114	N/A	-	scaffold_7:240846-241342		
N	16	183330	N/A	-0.912	N/A	-	scaffold_7:688697-690175		
N	16	41769	N/A	-0.5886	N/A	-	scaffold_8:954220-955782		
N	16	49708	N/A	-0.7396	N/A	Ribosomal protein L14	scaffold_9:1311196-1311807		
N	16	42232	N/A	-0.9876	N/A	-	scaffold_9:637811-638218		
N	17	36031	N/A	-0.4176	N/A	Putative GroEL-like chaperone, ATPase	scaffold_1:2084245-2086051		
N	17	130307	N/A	-0.737	N/A	RNA-binding protein required for biogenesis of the ribosomal 60S subunit	scaffold_1:2189615-2192590		
N	17	206151	N/A	-0.4559	N/A	Small GTP-binding protein domain	scaffold_1:2880115-2881246		
N	17	133810	N/A	-0.6472	N/A	FAD dependent oxidoreductase	scaffold_1:3693348-3694685		
N	17	143807	N/A	-0.4892	N/A	-	scaffold_10:867563-867923		
N	17	187424	N/A	-0.3769	N/A	defender against cell death protein	scaffold_10:911504-912138		
N	17	43537	N/A	-0.5596	N/A	hypothetical protein; Interpro desc: Peptidase M24 and Histone H4	scaffold_11:1532146-1532838		
N	17	54435	N/A	-0.9435	N/A	Ras small GTPase, Ras type	scaffold_12:17078-18391		
N	17	214079	N/A	-0.4968	N/A	translation initiation factor eIF-6	scaffold_16:761858-762891		
N	17	37132	N/A	-0.3157	N/A	prolyl-4-hydroxylase	scaffold_2:1987414-1988354		
N	17	177427	N/A	-0.337	N/A	hypothetical protein with predicted Sir2 and Appr-1-p domains; KOG Class: Chromatin structure and dynamics; KOG Id: 2633; KOG Description: Hismacro and SEC14 domain-containing proteins	scaffold_3:209602-211410		
N	17	37834	N/A	-0.3523	N/A	Mitochondrial import inner membrane translocase,	scaffold_3:579270-580063		
N	17	177722	N/A	-0.7269	N/A	Uroporphyrinogen III synthase HEM4	scaffold_3:743765-744833		
N	17	47841	N/A	-0.5082	N/A	-	scaffold_4:474963-476287		
N	17	179208	N/A	-0.463	N/A	Hypothetical RING finger domain protein	scaffold_4:667629-668286	131	
N	17	47870	N/A	-0.5134	N/A	-	scaffold_4:673093-674046	131	
N	17	39830	N/A	-0.727	N/A	related to patatin-like phospholipase	scaffold_5:938734-940343		
N	17	183005	N/A	-0.5291	N/A	related to extracellular arylsulfatase of Neurospora crassa	scaffold_6:1322000-1323999		
N	17	41962	N/A	-0.4434	N/A	Small nuclear ribonucleoprotein (snRNP) Sm core protein	scaffold_8:1542890-1543669		
N	17	53828	N/A	-0.5029	N/A	Hypothetical proteasome maturation factor	scaffold_8:995388-996368		
N	18	35811	N/A	-0.4596	N/A	Deduced amino acid sequence shares identity with ribose methyltransferase that modifies a functionally critical, conserved nucleotide in mitochondrial 21S rRNA.	scaffold_1:1429247-1430740		
N	18	129773	N/A	-0.8557	N/A	-	scaffold_1:1724306-1730217		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
N	18	55402	N/A	-0.4664	N/A	-	scaffold_1:2265789-2272335		
N	18	46719	N/A	-0.7609	N/A	Candidate multiple RNA-binding domain-containing protein.	scaffold_1:2928330-2931164		
N	18	196738	N/A	-0.4787	N/A	Signaling protein	scaffold_1:3069807-3076139		
N	18	172697	N/A	-0.6988	N/A	-	scaffold_1:3494366-3494866		
N	18	36502	N/A	-0.5841	N/A	hypothetical cytochrome p-450	scaffold_1:3779403-3780817		
N	18	171222	N/A	-0.6681	N/A	-	scaffold_1:3828203-3830869		
N	18	212190	N/A	-0.2939	N/A	Importin-beta	scaffold_10:1763159-1766876		
N	18	187288	N/A	-0.7898	N/A	-	scaffold_10:349104-350670		
N	18	187258	N/A	-0.6006	N/A	-	scaffold_10:696225-699711		
N	18	43406	N/A	-0.4742	N/A	Predicted Phytoene/squalene synthetase	scaffold_11:1162868-1164124		
N	18	43431	N/A	-0.4964	N/A	-	scaffold_11:1238780-1239403		
N	18	142826	N/A	-0.4802	N/A	Ribosomal protein L27	scaffold_11:253032-253637		
N	18	190142	N/A	-0.6731	N/A	Hypothetical RNA polymerase subunit	scaffold_12:206878-208014		
N	18	118599	N/A	-0.5183	N/A	Non-ribosomal peptide synthetase	scaffold_12:951451-967247		
N	18	191089	N/A	-0.6418	N/A	Hypothetical.N-acetyltransferase domain (GCN5)	scaffold_13:75612-76362		
N	18	129990	N/A	-0.7028	N/A	FOG: PPR repeat	scaffold_13:782527-785049		
N	18	50589	N/A	-0.4355	N/A	Putative Ubiquitin-conjugating enzymes, SUMO	scaffold_13:866084-866812		
N	18	213477	N/A	-0.5103	N/A	-	scaffold_14:292853-294568		
N	18	192425	N/A	-0.6121	N/A	-	scaffold_16:704845-705791		
N	18	193767	N/A	-0.5031	N/A	Predicted methyltransferase	scaffold_18:156516-157795		
N	18	193596	N/A	-0.5957	N/A	Pyridoxal-5′-phosphate-dependent enzyme	scaffold_18:438212-439739		
N	18	206719	N/A	-0.7286	N/A	Hypothetical protein with Zn-finger, Tim10/DDP type	scaffold_2:1108741-1109094		
N	18	37122	N/A	-0.5267	N/A	Dynactin, subunit p25	scaffold_2:1959345-1960030		
N	18	36655	N/A	-0.4754	N/A	Hypothetical peptidase (EC 3.5.1.32)	scaffold_2:274549-275835		
N	18	175410	N/A	-0.625	N/A	Peptidase	scaffold_2:360046-365417		
N	18	124716	N/A	-0.5512	N/A	hypothetical protein with RCC1 domain	scaffold_2:649837-650985		
N	18	195249	N/A	-0.5715	N/A	-	scaffold_24:41016-42136		
N	18	55738	N/A	-0.5216	N/A	Multifunctional pyrimidine synthesis protein CAD (pyrABCN)	scaffold_3:1680710-1687603		
N	18	176406	N/A	-0.5639	N/A	Deduced amino acid sequence shares identity with the Saccharomyces cerevisiae NHP2 gene product; a nuclear protein related to mammalian high mobility group (HMG) proteins, essential for function of H/ACA-type snoRNPs, which are involved in 18S rRNA processing.	scaffold_3:1868724-1869303		
N	18	37780	N/A	-0.7153	N/A	-	scaffold_3:410807-412090		
N	18	176803	N/A	-0.4928	N/A	-	scaffold_3:601498-602451		
N	18	39964	N/A	-0.6184	N/A	Conserved ATP/GTP binding protein	scaffold_5:1347405-1348488		
N	18	209768	N/A	-0.6093	N/A	Hypothetical protein of the Ribonuclease III supefamily	scaffold_5:1718857-1719825		
N	18	199877	N/A	-0.4232	N/A	hypothetical WD-40 repeat protein and G-protein β, normally coordinating multi-protein complex assemblies; KOG Class: Chromatin structure and dynamics; KOG Id: 1009; KOG Description: Chromatin assembly complex 1 subunit B/CAC2 (contains WD40 repeats)	scaffold_5:460311-462725		
N	18	39846	N/A	-0.6993	N/A	Predicted translation product shares amino acid sequence identity with the Saccharomyces cerevisiae RRP40 gene product; a protein involved in rRNA processing; component of the exosome 3->5 exonuclease complex.	scaffold_5:982316-983155		
N	18	40531	N/A	-0.3658	N/A	Citron-like	scaffold_6:832661-838291		
N	18	56391	N/A	-0.4311	N/A	-	scaffold_7:239172-240627		
N	18	118888	N/A	-0.4251	N/A	-	scaffold_7:657777-662217		
N	18	41880	N/A	-0.539	N/A	FAD dependent oxidoreductase	scaffold_8:1289285-1292029		
O	1	46836	N/A	0.4239	N/A	Short-chain dehydrogenase/reductase SDR	scaffold_1:3616412-3617203		
O	1	211758	N/A	0.3258	N/A	-	scaffold_10:87978-89933	132	
O	1	42599	N/A	0.4877	N/A	-	scaffold_10:93355-95382	132	
O	1	132773	N/A	0.3423	N/A	Cytochrome P450	scaffold_11:1396865-1398325		
O	1	43321	N/A	0.3883	N/A	-	scaffold_11:876875-877510		
O	1	189760	N/A	0.3374	N/A	Major facilitator superfamily	scaffold_12:746934-748771		
O	1	190592	N/A	0.369	N/A	Major facilitator superfamily	scaffold_13:126130-127856		
O	1	46236	N/A	0.3846	N/A	Putative citrate synthase (possibly bacterial origin)	scaffold_1409:129-1003		
O	1	44835	N/A	0.2576	N/A	-	scaffold_15:567659-568660		
O	1	45060	N/A	0.3354	N/A	-	scaffold_16:332835-333200		
O	1	45301	N/A	0.3	N/A	-	scaffold_17:170153-172191		
O	1	45442	N/A	0.3564	N/A	-	scaffold_17:682463-683429		
O	1	119967	N/A	0.2941	N/A	-	scaffold_17:7626-10255		
O	1	194405	N/A	0.2697	N/A	-	scaffold_19:503218-503937		
O	1	36861	N/A	0.3863	N/A	hypothetical extracellular protein	scaffold_2:1056624-1057046		
O	1	175057	N/A	0.2419	N/A	Major facilitator superfamily	scaffold_2:1145309-1146909		
O	1	173004	N/A	0.2529	N/A	Predicted hydrolase related to dienelactone hydrolase	scaffold_2:133774-134592		
O	1	37507	N/A	0.4556	N/A	-	scaffold_2:3561453-3562273		
O	1	37534	N/A	0.2744	N/A	-	scaffold_2:3636552-3637094		
O	1	46038	N/A	0.2193	N/A	hypothetical zinc-containing alcohol dehydrogenase	scaffold_21:273687-274825		
O	1	46047	N/A	0.3321	N/A	Cytochrome P450	scaffold_22:16672-18583		
O	1	176194	N/A	0.3473	N/A	Fungal specific transcription factor	scaffold_3:2713336-2714808		
O	1	177290	N/A	0.3473	N/A	-	scaffold_3:49624-50952	133	

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
O	1	47208	N/A	0.5495	N/A	N-Acetylglucosamine kinase	scaffold_3:51851-54066	133	
O	1	46208	N/A	0.4509	N/A	-	scaffold_333:21-834		
O	1	179079	N/A	0.3099	N/A	Putative polyketide synthase	scaffold_4:1055222-1063904		
O	1	140386	N/A	0.2696	N/A	Hypothetical monosaccharide transporter	scaffold_4:18349-20309		
O	1	178173	N/A	0.3337	N/A	-	scaffold_4:2415880-2417366		
O	1	142934	N/A	0.3184	N/A	Protein kinase	scaffold_5:1250726-1251385		
O	1	40928	N/A	0.4701	N/A	Nitrilase/cyanide hydratase	scaffold_7:97622-98800		
O	1	186640	N/A	0.2517	N/A	Hypothetical isoprenylcysteine carboxyl methyltransferase	scaffold_9:1359527-1360423		
O	1	186153	N/A	0.3145	N/A	-	scaffold_9:842773-844222		
O	2	35388	N/A	0.3869	N/A	related to tannase	scaffold_1:74568-76277		
O	2	43482	N/A	0.4922	N/A	putative amine oxidase	scaffold_11:1388864-1389973		
O	2	43335	N/A	0.3746	N/A	-	scaffold_11:926769-927113		
O	2	43929	N/A	0.4386	N/A	Hypothetical dehydrogenase	scaffold_12:1100843-1101706		
O	2	43697	N/A	0.2715	N/A	-	scaffold_12:409340-410905		
O	2	190471	N/A	0.3111	N/A	putative extracellular tannase and feruloyl esterase	scaffold_13:491502-493121		
O	2	190306	N/A	0.38	N/A	-	scaffold_13:77139-77491		
O	2	191411	N/A	0.3638	N/A	-	scaffold_14:770266-771441		
O	2	124656	N/A	0.2572	N/A	Glucose/ribitol dehydrogenase	scaffold_15:229114-230582		
O	2	122237	N/A	0.3644	N/A	Major facilitator superfamily	scaffold_2:1502621-1504226		
O	2	174539	N/A	0.3033	N/A	-	scaffold_2:1822730-1825299		
O	2	46084	N/A	0.3002	N/A	-	scaffold_22:112298-112972		
O	2	177034	N/A	0.3193	N/A	-	scaffold_3:2281469-2282110		
O	2	55820	N/A	0.4418	N/A	-	scaffold_3:2658316-2659735		
O	2	178499	N/A	0.368	N/A	Homogentisate 1,2-dioxygenase	scaffold_4:169987-171814		
O	2	179356	N/A	0.4459	N/A	unknown, SignalP suggest secretion	scaffold_4:1809011-1809901		
O	2	39348	N/A	0.4152	N/A	Esterase/lipase/thioesterase	scaffold_4:2233178-2234095		
O	2	39368	N/A	0.305	N/A	Major facilitator superfamily	scaffold_4:2292754-2294441		
O	2	179427	N/A	0.3306	N/A	-	scaffold_4:44818-46260		
O	2	40101	N/A	0.4217	N/A	-	scaffold_5:1864865-1865260		
O	2	40205	N/A	0.3372	N/A	-	scaffold_5:2209554-2211450		
O	2	181869	N/A	0.2768	N/A	diacylglycerol acyltransferase	scaffold_6:1010697-1011248		
O	2	40729	N/A	0.3291	N/A	-	scaffold_6:1474128-1474445		
O	2	40383	N/A	0.3012	N/A	putative transmembrane protein	scaffold_6:294471-295388		
O	2	40471	N/A	0.4792	N/A	hypothetical tannase and feruloyl esterase	scaffold_6:665105-667369		
O	2	184208	N/A	0.3145	N/A	Molybdenum cofactor sulfurase	scaffold_7:1015105-1016586	134	
O	2	41225	N/A	0.3566	N/A	-	scaffold_7:1021580-1022655	134	
O	2	124357	N/A	0.3943	N/A	-	scaffold_7:1051439-1052721		
O	2	41375	N/A	0.3841	N/A	-	scaffold_7:1572282-1572802		
O	2	41831	N/A	0.4092	N/A	Hypothetical aromatic ring-opening dioxygenase	scaffold_8:1135878-1136842		
O	2	42243	N/A	0.327	N/A	putative tannase and feruloyl esterase	scaffold_9:661090-662673		
O	2	135959	N/A	0.3031	N/A	-	scaffold_9:882280-883131		
O	3	171384	N/A	0.3704	N/A	Aromatic-ring hydroxylase	scaffold_1:1615007-1616589		
O	3	206358	N/A	0.359	N/A	-	scaffold_1:3639970-3641266		
O	3	131667	N/A	0.4237	N/A	Multicopper oxidase, type 1	scaffold_1:3740943-3742598		
O	3	132972	N/A	0.3465	N/A	-	scaffold_10:62925-64451		
O	3	43394	N/A	0.3774	N/A	-	scaffold_11:1127332-1128513		
O	3	43529	N/A	0.321	N/A	ABC transporter	scaffold_11:1502225-1506245		
O	3	143030	N/A	0.3422	N/A	Haloacid dehalogenase-like hydrolase	scaffold_12:1185502-1186128		
O	3	120296	N/A	0.3592	N/A	Fungal specific transcription factor	scaffold_12:199233-201054		
O	3	128821	N/A	0.413	N/A	Fungal specific transcription factor	scaffold_12:226697-232235		
O	3	54636	N/A	0.3984	N/A	-	scaffold_13:893205-894425		
O	3	44840	N/A	0.3667	N/A	Ankyrin	scaffold_15:581763-583676		
O	3	192754	N/A	0.352	N/A	-	scaffold_16:807121-808953		
O	3	36751	N/A	0.2932	N/A	-	scaffold_2:638851-639314		
O	3	126350	N/A	0.2305	N/A	-	scaffold_26:26607-27417		
O	3	38239	N/A	0.3392	N/A	-	scaffold_3:2035834-2037894		
O	3	47702	N/A	0.4884	N/A	Major facilitator superfamily	scaffold_3:3316293-3317693		
O	3	37765	N/A	0.4408	N/A	-	scaffold_3:364920-366207		
O	3	39398	N/A	0.3827	N/A	-	scaffold_4:2395143-2396168		
O	3	133055	N/A	0.2704	N/A	Cytochrome P450 CYP2 subfamily	scaffold_4:336508-337298		
O	3	38789	N/A	0.2686	N/A	-	scaffold_4:364595-366252		
O	3	200103	N/A	0.5193	N/A	-	scaffold_5:1178977-1182310		
O	3	184530	N/A	0.2911	N/A	Peptidase	scaffold_8:1315857-1316462		
O	3	42427	N/A	0.406	N/A	hypothetical protein with esterase/lipase/thioesterase and signal peptide motifs	scaffold_9:1199607-1200644		
O	3	126926	N/A	0.456	N/A	hypothetical protein with esterase/lipase/thioesterase motifs	scaffold_9:1210181-1210845		
O	3	42513	N/A	0.2753	N/A	-	scaffold_9:1486913-1487856		
O	4	35716	N/A	0.3161	N/A	regulatory protein brlA , morphology	scaffold_1:1126973-1128250		
O	4	36244	N/A	0.2776	N/A	-	scaffold_1:3011023-3011639		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
O	4	172038	N/A	0.3321	N/A	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_1:70636-71525		
O	4	141677	N/A	0.3421	N/A	(pgal) polygalacturonase I	scaffold_1:918865-920082		
O	4	43483	N/A	0.3062	N/A	Aromatic-ring hydroxylase	scaffold_11:1391210-1392791		
O	4	43969	N/A	0.2837	N/A	hypothetical urea amidolyase (EC 6.3.4.6)	scaffold_12:1216665-1218518		
O	4	44928	N/A	0.3766	N/A	-	scaffold_15:876650-878039		
O	4	36643	N/A	0.5304	N/A	-	scaffold_2:236302-236658		
O	4	37297	N/A	0.4136	N/A	Protein kinase	scaffold_2:2878674-2879724		
O	4	37370	N/A	0.3186	N/A	-	scaffold_2:3130057-3132726		
O	4	139164	N/A	0.4007	N/A	putative carboxylesterase	scaffold_2:71533-73191		
O	4	36796	N/A	0.3604	N/A	-	scaffold_2:805991-806560		
O	4	47931	N/A	0.3836	N/A	Esterase/lipase/thioesterase	scaffold_4:1097214-1098233		
O	4	123599	N/A	0.2932	N/A	Major facilitator superfamily	scaffold_4:132292-133747		
O	4	178901	N/A	0.4247	N/A	-	scaffold_4:1642382-1645264		
O	4	40157	N/A	0.375	N/A	-	scaffold_5:2070864-2071250		
O	4	181201	N/A	0.2829	N/A	Beta-ketoacyl synthase	scaffold_5:2229939-2231991		
O	4	39702	N/A	0.3371	N/A	hypothetical SH3 domain protein	scaffold_5:479674-481529		
O	4	139884	N/A	0.3746	N/A	-	scaffold_8:640163-642173		
O	4	42120	N/A	0.3516	N/A	-	scaffold_9:300258-300902		
O	5	212709	N/A	0.4337	N/A	-	scaffold_11:1468774-1469720		
O	5	189326	N/A	0.3417	N/A	Putative protein kinase domain	scaffold_11:1619097-1620383		
O	5	190154	N/A	0.2759	N/A	Aromatic-ring hydroxylase	scaffold_12:1013069-1014541		
O	5	44975	N/A	0.3164	N/A	Zinc-containing alcohol dehydrogenase	scaffold_16:58010-59719		
O	5	45726	N/A	0.5311	N/A	-	scaffold_19:276271-277521		
O	5	36888	N/A	0.3351	N/A	Aminotransferase	scaffold_2:1151241-1152569		
O	5	173459	N/A	0.2761	N/A	-	scaffold_2:227489-228986		
O	5	38063	N/A	0.4267	N/A	putative steroid monooxygenase	scaffold_3:1331521-1332764		
O	5	136118	N/A	0.4748	N/A	-	scaffold_3:3330414-3331518		
O	5	137298	N/A	0.4238	N/A	-	scaffold_4:2017983-2018411		
O	5	38687	N/A	0.4206	N/A	Major facilitator superfamily	scaffold_4:22140-23832		
O	5	40261	N/A	0.3939	N/A	hypothetical α-glucosidase (GH family 31)	scaffold_5:2353925-2356280		
O	5	40868	N/A	0.4083	N/A	Pectinesterase	scaffold_6:1925619-1926488		
O	5	210777	N/A	0.3814	N/A	-	scaffold_7:1602318-1603289		
O	6	35366	N/A	0.4682	N/A	-	scaffold_1:17525-18007		
O	6	170788	N/A	0.3028	N/A	-	scaffold_1:3349459-3350634		
O	6	35662	N/A	0.4659	N/A	-	scaffold_1:973870-975863		
O	6	134351	N/A	0.324	N/A	-	scaffold_10:133585-134952		
O	6	50157	N/A	0.4015	N/A	hypothetical Amino acid/polyamine transporter I	scaffold_11:935296-937048		
O	6	131671	N/A	0.2695	N/A	-	scaffold_12:106498-108170		
O	6	43761	N/A	0.2583	N/A	-	scaffold_12:597270-597707		
O	6	43817	N/A	0.3092	N/A	Ankyrin	scaffold_12:771580-772481		
O	6	190541	N/A	0.3278	N/A	Serine/threonine protein kinase	scaffold_13:578999-579545		
O	6	44402	N/A	0.4486	N/A	Cytochrome c heme-binding site	scaffold_14:144331-144897		
O	6	50936	N/A	0.3376	N/A	putative aldo/keto reductase	scaffold_16:15394-16423		
O	6	45554	N/A	0.3253	N/A	-	scaffold_18:390437-391143		
O	6	214657	N/A	0.4323	N/A	-	scaffold_19:268653-269231		
O	6	51385	N/A	0.3735	N/A	Hypothetical acetolactate synthase	scaffold_19:505095-506908		
O	6	38313	N/A	0.4067	N/A	-	scaffold_3:2280001-2280609		
O	6	38569	N/A	0.2339	N/A	-	scaffold_3:3278777-3280114		
O	6	126958	N/A	0.2554	N/A	-	scaffold_4:1595066-1595524		
O	6	179368	N/A	0.2979	N/A	Major facilitator superfamily	scaffold_4:2117247-2118610		
O	6	39361	N/A	0.4683	N/A	-	scaffold_4:2267130-2267832		
O	6	124205	N/A	0.2946	N/A	Related to 4-hydroxyphenylpyruvate dioxygenase	scaffold_5:2057097-2058388		
O	6	40225	N/A	0.4696	N/A	NADH:flavin oxidoreductase/NADH oxidase	scaffold_5:2259410-2260745		
O	6	181662	N/A	0.3905	N/A	Amidase	scaffold_5:2404554-2405207		
O	6	39737	N/A	0.2838	N/A	-	scaffold_5:622594-623553		
O	6	40508	N/A	0.4635	N/A	Tyrosine protein kinase, active site	scaffold_6:767962-768834		
O	6	184074	N/A	0.4997	N/A	-	scaffold_7:1178287-1182895		
O	6	41901	N/A	0.5613	N/A	-	scaffold_8:1358849-1359550		
O	6	211595	N/A	0.3605	N/A	related to extracellular GH family 61 endo-1,4-beta-glucanase of Trichoderma reesei	scaffold_9:1138402-1139238		
O	7	119851	N/A	0.3876	N/A	Putative gene involved in fumonisin B2 biosynthesis, aminotransferase	scaffold_1:2009952-2012602		
O	7	171904	N/A	0.4045	N/A	Predicted transporter (major facilitator superfamily)	scaffold_1:3769540-3771851		
O	7	35595	N/A	0.3774	N/A	Hypothetical fatty acid synthase or polyketide synthase subunit	scaffold_1:786155-787487		
O	7	42641	N/A	0.3757	N/A	Hypothetical SUR2-type hydroxylase/desaturase, catalytic region	scaffold_10:220386-221402		
O	7	42861	N/A	0.504	N/A	Phosphoesterase	scaffold_10:979750-981226		
O	7	43919	N/A	0.2895	N/A	-	scaffold_12:1082360-1083720		
O	7	143971	N/A	0.5683	N/A	Zn-finger, FYVE type	scaffold_12:311034-311198		
O	7	54490	N/A	0.4103	N/A	related to cellulose 1,4-beta-cellobiosidase II of Trichoderm reesei and Talaromyces emersonii	scaffold_12:588704-590588		
O	7	45030	N/A	0.4305	N/A	-	scaffold_16:249365-250221		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
O	7	51317	N/A	0.3753	N/A	-	scaffold_18:475223-478705		
O	7	36620	N/A	0.3059	N/A	putative FAD/FMN-containing dehydrogenase (COG0277) with signal peptide motif	scaffold_2:168903-170609		
O	7	47031	N/A	0.2891	N/A	Esterase/lipase/thioesterase	scaffold_2:1843235-1844767		
O	7	195091	N/A	0.3124	N/A	Zinc-containing alcohol dehydrogenase	scaffold_21:246896-247894		
O	7	143038	N/A	0.2819	N/A	Tyrosine protein kinase	scaffold_22:30970-31458		
O	7	37982	N/A	0.5057	N/A	-	scaffold_3:1057437-1058363		
O	7	125795	N/A	0.372	N/A	-	scaffold_3:168547-169352		
O	7	52725	N/A	0.5665	N/A	Flavin-containing monooxygenase	scaffold_3:2633659-2636242		
O	7	37737	N/A	0.2943	N/A	-	scaffold_3:284856-285516		
O	7	119775	N/A	0.346	N/A	putative GH family 71 endo-1,3-alpha-glucanase	scaffold_3:436040-438136		
O	7	177717	N/A	0.3315	N/A	Candidate RTA1 domain protein. Mb bound, repsonse to xenobiotics	scaffold_3:482543-483453		
O	7	38987	N/A	0.2864	N/A	-	scaffold_4:1046287-1047876		
O	7	39113	N/A	0.2904	N/A	-	scaffold_4:1448782-1449223		
O	7	52995	N/A	0.3667	N/A	-	scaffold_4:1666033-1666626		
O	7	39267	N/A	0.4553	N/A	-	scaffold_4:1964740-1965822		
O	7	40668	N/A	0.339	N/A	-	scaffold_6:1274416-1276267		
O	7	181749	N/A	0.2347	N/A	Major facilitator superfamily	scaffold_6:1329708-1330925		
O	7	49430	N/A	0.614	N/A	Hypothetical arginase	scaffold_8:1419860-1421480		
O	7	42086	N/A	0.3959	N/A	-	scaffold_9:184324-184765		
O	7	42216	N/A	0.4676	N/A	Cytochrome P450	scaffold_9:592372-594400		
O	8	188035	N/A	0.3116	N/A	-	scaffold_10:85725-87107		
O	8	189853	N/A	0.3372	N/A	-	scaffold_12:1109726-1116084		
O	8	121921	N/A	0.5913	N/A	-	scaffold_12:458545-460177		
O	8	37292	N/A	0.484	N/A	-	scaffold_2:2856863-2859323		
O	8	45866	N/A	0.4237	N/A	-	scaffold_20:92877-95024		
O	8	177858	N/A	0.4188	N/A	hypothetical short chain dehydrogenase	scaffold_3:190080-190968		
O	8	176409	N/A	0.3464	N/A	hypothetical citrate synthase	scaffold_3:234697-236309		
O	8	39024	N/A	0.3517	N/A	Phospholipase/carboxyhydrolase	scaffold_4:1160323-1161232		
O	8	40881	N/A	0.3452	N/A	-	scaffold_6:1968126-1968902		
O	8	195367	N/A	0.3622	N/A	Flavin-containing monooxygenase FMO	scaffold_81:849-1225		
O	8	185974	N/A	0.4202	N/A	Cytochrome P450	scaffold_9:1375343-1377059		
O	8	211527	N/A	0.2716	N/A	-	scaffold_9:849250-850889		
O	9	35415	N/A	0.4362	N/A	Ca2+-modulated nonselective cation channel polycystin	scaffold_1:162164-164824		
O	9	35934	N/A	1.0004	N/A	-	scaffold_1:1809815-1810532		
O	9	206339	N/A	1.9042	N/A	Haem peroxidase, plant/fungal/bacterial	scaffold_1:3406482-3408770		
O	9	138352	N/A	0.3587	N/A	-	scaffold_1:978329-978659		
O	9	128601	N/A	1.9699	N/A	Polyketide synthase	scaffold_15:700665-712297	135	
O	9	191998	N/A	2.9565	N/A	-	scaffold_15:713461-714065	135	
O	9	44878	N/A	2.4657	N/A	hypothetical cytochrome P450 alkane hydroxylase	scaffold_15:717358-719025	135	
O	9	193613	N/A	0.3037	N/A	Amino acid/polyamine transporter	scaffold_18:403200-404965		
O	9	37655	N/A	0.3811	N/A	Predicted hydrolase	scaffold_3:11155-11715		
O	9	52617	N/A	0.3587	N/A	Aromatic-ring hydroxylase	scaffold_3:1555675-1557354		
O	9	37925	N/A	0.5227	N/A	-	scaffold_3:878370-879224		
O	9	48052	N/A	0.7171	N/A	Probable glyoxylase	scaffold_4:1916277-1917281		
O	9	39317	N/A	0.2753	N/A	-	scaffold_4:2130569-2131623		
O	9	39633	N/A	0.2753	N/A	-	scaffold_5:227758-228261		
O	9	40254	N/A	0.4365	N/A	Hypothetical glucose oxidase (EC 1.1.3.4)	scaffold_5:2337616-2339511		
O	9	126673	N/A	0.3027	N/A	Chloroperoxidase	scaffold_7:1670572-1671261		
O	9	42507	N/A	0.3823	N/A	Fungal transcriptional regulatory protein	scaffold_9:1432147-1434041		
O	9	201885	N/A	0.5416	N/A	Alkyl hydroperoxide reductase/peroxiredoxin/peroxisomal	scaffold_9:265556-266340		
O	9	143614	N/A	0.3169	N/A	Actin-binding, cofilin/tropomyosin type	scaffold_9:65422-65958		
O	10	35364	N/A	0.3504	N/A	Major facilitator superfamily	scaffold_1:13393-15015		
O	10	35913	N/A	0.4176	N/A	-	scaffold_1:1747270-1747888		
O	10	196457	N/A	0.5108	N/A	-	scaffold_1:2114380-2114976		
O	10	51955	N/A	0.2578	N/A	-	scaffold_1:2401640-2401975		
O	10	170610	N/A	0.3339	N/A	Cytochrome P450	scaffold_1:3049472-3050847		
O	10	46788	N/A	0.2986	N/A	-	scaffold_1:3269494-3271413		
O	10	42621	N/A	0.3254	N/A	Glutamine amidotransferase class-I	scaffold_10:170045-170887		
O	10	188912	N/A	0.3315	N/A	Major facilitator superfamily	scaffold_11:1283566-1285332		
O	10	43489	N/A	0.5861	N/A	-	scaffold_11:1403960-1405668		
O	10	125481	N/A	0.3152	N/A	-	scaffold_11:1606647-1607763		
O	10	43295	N/A	0.2287	N/A	-	scaffold_11:810613-811258		
O	10	212866	N/A	0.6133	N/A	-	scaffold_12:349228-351190		
O	10	43851	N/A	0.4604	N/A	-	scaffold_12:862311-862883		
O	10	43992	N/A	0.3388	N/A	-	scaffold_13:69366-70852		
O	10	44469	N/A	0.3384	N/A	Aromatic-ring hydroxylase	scaffold_14:391965-393762		
O	10	44483	N/A	0.4794	N/A	-	scaffold_14:435852-436345		
O	10	191883	N/A	0.6454	N/A	putative extracellular carboxylesterase	scaffold_15:863427-865016		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
O	10	136764	N/A	0.3128	N/A	Chloroperoxidase	scaffold_16:254452-255181		
O	10	36884	N/A	0.2913	N/A	-	scaffold_2:1139975-1141307		
O	10	175466	N/A	0.2905	N/A	Oxidoreductase, N-terminal	scaffold_2:1930573-1932180		
O	10	139245	N/A	0.3265	N/A	PEP-utilising enzyme	scaffold_20:307468-312030		
O	10	45961	N/A	0.3796	N/A	Intradiol ring-cleavage dioxygenase	scaffold_21:47421-48479		
O	10	37999	N/A	0.3373	N/A	-	scaffold_3:1097040-1097472		
O	10	133512	N/A	0.3213	N/A	-	scaffold_3:1264961-1266161		
O	10	207841	N/A	0.3136	N/A	-	scaffold_3:1531426-1533034		
O	10	47221	N/A	0.3678	N/A	Peptidase, eukaryotic cysteine peptidase active site	scaffold_3:199224-200585		
O	10	38636	N/A	0.3043	N/A	-	scaffold_3:3469338-3470927		
O	10	208760	N/A	0.288	N/A	(pelC) pectin lyase C	scaffold_4:1109601-1110943		
O	10	39016	N/A	0.3	N/A	-	scaffold_4:1130750-1131170		
O	10	40054	N/A	0.4943	N/A	hypothetical protein; KOG Class: Chromatin structure and dynamics	scaffold_5:1690596-1691852		
O	10	181473	N/A	0.3331	N/A	FMN-dependent α-hydroxy acid dehydrogenase	scaffold_5:2437658-2439182		
O	10	48286	N/A	0.7271	N/A	hypothetical NADH:flavin oxidoreductase/NADH oxidase	scaffold_5:451628-452737		
O	10	184254	N/A	0.297	N/A	-	scaffold_7:1098212-1098727		
O	10	124892	N/A	0.2721	N/A	-	scaffold_7:1536828-1537388		
O	10	53548	N/A	0.3694	N/A	-	scaffold_7:19366-19868		
O	10	41210	N/A	0.2647	N/A	Thioesterase superfamily	scaffold_7:970845-971246		
O	10	41898	N/A	0.3351	N/A	-	scaffold_8:1343223-1344013		
O	10	41638	N/A	0.4674	N/A	related to serine carboxypepidase of Aspergillus saitoi	scaffold_8:560832-562434		
O	10	41679	N/A	0.3101	N/A	-	scaffold_8:674136-674964		
O	10	184510	N/A	0.3379	N/A	Cytochrome P450	scaffold_8:920619-922231		
O	10	42034	N/A	0.3024	N/A	Formate/nitrite transporter	scaffold_9:29225-30260		
O	10	42219	N/A	0.5449	N/A	-	scaffold_9:603201-604402		
P	1	205884	N/A	N/A	-0.2941	-	scaffold_1:1916868-1918231		
P	1	127221	N/A	N/A	-0.3808	-	scaffold_1:3671001-3671396		
P	1	43007	N/A	N/A	-0.5278	-	scaffold_10:1837724-1838803		
P	1	43093	N/A	N/A	-0.488	-	scaffold_11:129507-130773		
P	1	127140	N/A	N/A	-0.4187	-	scaffold_11:881709-882294		
P	1	213737	N/A	N/A	-0.3269	-	scaffold_15:247564-249136		
P	1	191797	N/A	N/A	-0.4388	Zn-finger-like, PHD finger	scaffold_15:322854-325772		
P	1	45195	N/A	N/A	-0.2956	-	scaffold_16:771009-772113		
P	1	55587	N/A	N/A	-0.5092	-	scaffold_2:1891913-1894712		
P	1	47040	N/A	N/A	-0.2941	Major facilitator superfamily	scaffold_2:1907098-1908771		
P	1	140003	N/A	N/A	-0.2903	Fungal specific transcription factor	scaffold_2:290219-292133		
P	1	197796	N/A	N/A	-1.146	Collagens	scaffold_2:3238553-3241465		
P	1	195043	N/A	N/A	-0.2779	Hypothetical non-ribosomal peptide synthetase. Shows some identity to the Penicillium nordicum ochratoxin A NRPS.	scaffold_21:16784-20159		
P	1	41071	N/A	N/A	-0.5433	-	scaffold_7:560243-563305		
P	1	185526	N/A	N/A	-0.2642	Hypothetical protein with Cytochrome c heme-binding site	scaffold_8:1307415-1308809		
P	1	54001	N/A	N/A	-0.5802	putative Hsp60	scaffold_9:1037566-1039478		
P	1	56666	N/A	N/A	-0.4233	hypothetical Zn-finger protein, C2H2 type domain	scaffold_9:339620-340671		
P	2	205400	N/A	N/A	-0.8581	Importin-beta, N-terminal	scaffold_1:244994-248127		
P	2	36196	N/A	N/A	-0.5041	Hypothetical sulphate anion transporter	scaffold_1:2800497-2801551		
P	2	133797	N/A	N/A	-0.3207	-	scaffold_10:299129-300279		
P	2	50359	N/A	N/A	-0.4597	Hypothetical. Hemebinding ?	scaffold_12:745503-746570		
P	2	50376	N/A	N/A	-0.3514	related to glucose oxidase	scaffold_12:888570-890537		
P	2	123814	N/A	N/A	-0.2868	Acyl-CoA oxidase	scaffold_12:985284-986435		
P	2	55081	N/A	N/A	-0.4411	Translation initiation factor 2C	scaffold_18:456212-459558		
P	2	194546	N/A	N/A	-0.3328	-	scaffold_19:517104-518260		
P	2	143049	N/A	N/A	-0.5817	Hypothetical protein with an RNA recognition motif	scaffold_4:1618349-1619272		
P	2	178369	N/A	N/A	-0.2676	Major facilitator superfamily	scaffold_4:2289469-2291289		
P	2	39767	N/A	N/A	-0.2613	hypothetical protein predicted to be a fungal transcriptional regulatory protein (N-terminal, has cystein-rich motif); KOG Class: Chromatin structure and dynamics; KOG Id: 1472; KOG Description: Histone acetyltransferase SAGA/ADA, catalytic subunit PCAF/GCN5 and related proteins	scaffold_5:719692-722327		
P	2	182803	N/A	N/A	-1.163	ABC transporter	scaffold_6:410516-415214		
P	3	127757	N/A	N/A	-0.4531	-	scaffold_1:941189-941719		
P	3	44261	N/A	N/A	-0.2367	Hypothetical splicing coactivator SRm160/300, subunit SRm300	scaffold_13:857983-860731		
P	3	45045	N/A	N/A	-0.4054	Myosin class II heavy chain	scaffold_16:287246-288872		
P	3	123074	N/A	N/A	-0.3743	-	scaffold_6:1713895-1715258		
P	3	41408	N/A	N/A	-0.2451	-	scaffold_7:1672585-1672980		
P	3	41772	N/A	N/A	-0.3241	-	scaffold_8:965252-965731		
P	4	35385	N/A	N/A	-0.3092	-	scaffold_1:63316-64128		
P	4	56946	N/A	N/A	-0.2944	Putative polyketide synthase	scaffold_11:1291712-1299626		
P	4	43864	N/A	N/A	-0.349	-	scaffold_12:915893-916636		
P	4	122811	N/A	N/A	-0.3468	-	scaffold_13:589892-591817		
P	4	192636	N/A	N/A	-0.3581	Monocarboxylate transporter	scaffold_16:225308-226682		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
P	4	194416	N/A	N/A	-0.2983	Related to alcohol dehydrogenase; EC 1.1.1.1; sequence similarity to Emericella nidulans	scaffold_19:346186-347610		
P	4	174228	N/A	N/A	-0.7491	-	scaffold_2:98734-99930		
P	4	138187	N/A	N/A	-0.2598	-	scaffold_20:249306-249692		
P	4	38352	N/A	N/A	-0.3256	-	scaffold_3:2406883-2407745		
P	4	40198	N/A	N/A	-0.2719	-	scaffold_5:2187230-2188241		
P	4	140802	N/A	N/A	-0.2957	Monocarboxylate transporter	scaffold_8:407145-408326		
P	5	35805	N/A	N/A	-0.5291	-	scaffold_1:1414297-1415219		
P	5	36285	N/A	N/A	-0.3496	-	scaffold_1:3144453-3145235		
P	5	141117	N/A	N/A	-0.3264	HPr serine phosphorylation site	scaffold_11:1677717-1679261		
P	5	43789	N/A	N/A	-0.4389	-	scaffold_12:670722-671814		
P	5	203521	N/A	N/A	-0.4559	Hypothetical protein containing a Kelch repeat	scaffold_13:355327-357921		
P	5	54616	N/A	N/A	-0.2451	Acetolactate synthase, small subunit	scaffold_13:790973-792016		
P	5	191260	N/A	N/A	-0.3189	Major facilitator superfamily	scaffold_14:687229-689198		
P	5	127419	N/A	N/A	-0.3724	ABC transporter	scaffold_21:4138-4705		
P	5	38522	N/A	N/A	-0.339	Molecular chaperones HSP70/HSC70	scaffold_3:3142807-3144926		
P	5	38638	N/A	N/A	-0.4374	Amino acid transporters	scaffold_3:3476295-3478329		
P	5	38947	N/A	N/A	-0.3921	-	scaffold_4:922299-923783		
P	5	38964	N/A	N/A	-0.4028	Peptidase M14, carboxypeptidase A	scaffold_4:977342-978441		
P	5	180382	N/A	N/A	-0.2982	-	scaffold_5:2329264-2330091		
P	5	210303	N/A	N/A	-0.4171	Hypothetical amino acyl-tRNA synthetase complex component.	scaffold_6:1573755-1575092		
P	5	186000	N/A	N/A	-0.3134	Amino acid/polyamine transporter	scaffold_9:884149-885774		
P	6	36202	N/A	N/A	-0.3227	-	scaffold_1:2868491-2869617		
P	6	35591	N/A	N/A	-0.3128	-	scaffold_1:774269-774715		
P	6	187856	N/A	N/A	-0.332	Hypothetical aldehyde dehydrogenase	scaffold_10:977732-979376		
P	6	44124	N/A	N/A	-0.4311	-	scaffold_13:467195-467677		
P	6	121803	N/A	N/A	-0.2873	K+ channel, two pore	scaffold_15:744738-746222		
P	6	213911	N/A	N/A	-0.3462	Aldehyde dehydrogenase	scaffold_16:289158-290715		
P	6	37117	N/A	N/A	-0.3828	-	scaffold_2:1947903-1948370		
P	6	173527	N/A	N/A	-0.3657	related to the extracellular pectin lyase C	scaffold_2:26610-27790		
P	6	40209	N/A	N/A	-0.4481	-	scaffold_5:2221220-2221900		
P	6	39654	N/A	N/A	-0.4	putative β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_5:292451-293662		
P	6	56715	N/A	N/A	-0.6866	Acetyl-CoA carboxylase	scaffold_9:1270900-1277897		
P	6	186516	N/A	N/A	-0.319	-	scaffold_9:601282-601908		
P	7	171880	N/A	N/A	-0.3751	Multicopper oxidase	scaffold_1:355236-357157		
P	7	35596	N/A	N/A	-0.3619	Phosphopantetheine-binding	scaffold_1:788862-789206		
P	7	44546	N/A	N/A	-0.3605	-	scaffold_14:634804-636703		
P	7	52616	N/A	N/A	-0.3076	hypothetical carboxylesterase	scaffold_3:1537264-1538940		
P	7	37659	N/A	N/A	-0.3208	-	scaffold_3:19179-20117		
P	7	38585	N/A	N/A	-0.2508	Glutamate-cysteine ligase catalytic subunit	scaffold_3:3327004-3329139		
P	7	37945	N/A	N/A	-0.444	-	scaffold_3:945851-948279		
P	7	39013	N/A	N/A	-0.2937	-	scaffold_4:1123895-1124588		
P	7	134585	N/A	N/A	-0.4378	-	scaffold_5:1681408-1682316		
P	7	133782	N/A	N/A	-0.432	Hypothetical protein with a MOSC domain	scaffold_5:2055410-2056573		
P	7	42010	N/A	N/A	-0.33	-	scaffold_8:1688773-1690170		
P	7	185196	N/A	N/A	-0.3552	Major facilitator superfamily	scaffold_8:272718-274768		
P	7	41619	N/A	N/A	-0.3869	Zinc-binding oxidoreductase	scaffold_8:503376-504543		
Q	1	119074	N/A	N/A	0.7778	WD40 repeat-containing protein	scaffold_1:173653-177890		
Q	1	140888	N/A	N/A	0.6791	Glutathione S-transferase	scaffold_1:1939027-1940906		
Q	1	170627	N/A	N/A	0.8924	-	scaffold_1:2034846-2035748		
Q	1	36035	N/A	N/A	0.8006	-	scaffold_1:2092445-2093337		
Q	1	172404	N/A	N/A	0.5927	Predicted fumarylacetoacetate hydralase	scaffold_1:2236946-2238083	136	
Q	1	46629	N/A	N/A	0.7765	-	scaffold_1:2238612-2239126	136	
Q	1	52069	N/A	N/A	0.6226	-	scaffold_1:3708916-3710227		
Q	1	206387	N/A	N/A	1.3108	(abfA) α-L-arabinofuranosidase abfA	scaffold_1:3865249-3867487		
Q	1	188030	N/A	N/A	0.2468	Major facilitator superfamily	scaffold_10:1903821-1905888		
Q	1	202429	N/A	N/A	0.758	-	scaffold_10:797609-799138		
Q	1	189097	N/A	N/A	1.6327	Related to pyruvate decarboxylase; EC 4.1.1.1	scaffold_11:1481513-1483231	137	
Q	1	121710	N/A	N/A	0.4713	Amidases	scaffold_11:1484023-1485864	137	
Q	1	212451	N/A	N/A	0.7171	Hypothetical NADH pyrophosphatase I of the Nudix family of hydrolases	scaffold_11:359966-361338		
Q	1	54329	N/A	N/A	1.0199	-	scaffold_11:398510-398869		
Q	1	54341	N/A	N/A	0.9285	hypothetical short chain dehydrogenase	scaffold_11:566017-567130		
Q	1	189450	N/A	N/A	0.4872	Heat shock protein DnaJ	scaffold_12:153040-154296		
Q	1	43685	N/A	N/A	0.7521	-	scaffold_12:367103-369219		
Q	1	128421	N/A	N/A	0.7374	FOG: WD40 repeat	scaffold_126:3034-3480		
Q	1	203625	N/A	N/A	0.9622	-	scaffold_13:636857-637375		
Q	1	191512	N/A	N/A	2.0583	Hypothetical enoyl-CoA hydratase (EC 4.2.1.17)	scaffold_14:105566-106452		
Q	1	50781	N/A	N/A	1.2598	related to Mitochondrial transport protein amc-1	scaffold_14:928999-930052		
Q	1	214375	N/A	N/A	0.7536	Fructose-1,6-bisphosphatase	scaffold_17:573551-574685		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	1	214391	N/A	N/A	0.7135	Permease of the major facilitator superfamily	scaffold_17:594448-596133		
Q	1	193991	N/A	N/A	0.8338	-	scaffold_18:319033-320003		
Q	1	194059	N/A	N/A	0.4789	related to acetamidase C (EC 3.5.1.4). Looks like it is actually two genes with different activities.	scaffold_18:440316-444222		
Q	1	45688	N/A	N/A	1.1161	Hypothetical alanine racemase	scaffold_19:170858-171964		
Q	1	206691	N/A	N/A	0.7867	Histidine kinase	scaffold_2:1036991-1038533		
Q	1	52109	N/A	N/A	0.7109	Fungal specific transcription factor	scaffold_2:186309-188434		
Q	1	52459	N/A	N/A	0.4497	Hypothetical peptidase	scaffold_2:3710712-3712694	138	
Q	1	52460	N/A	N/A	0.766	-	scaffold_2:3713074-3715555	138	
Q	1	194884	N/A	N/A	0.9897	-	scaffold_20:80646-81728		
Q	1	38054	N/A	N/A	0.828	Hypothetical Short-chain dehydrogenase/reductase SDR	scaffold_3:1306997-1308013		
Q	1	47520	N/A	N/A	0.464	hypothetical protein	scaffold_3:2184737-2186863		
Q	1	52520	N/A	N/A	1.1435	Hypothetical Short-chain dehydrogenase/reductase	scaffold_3:377287-378392		
Q	1	52585	N/A	N/A	0.9361	Ferric reductase, NADH/NADPH oxidase and related proteins	scaffold_3:918317-920121		
Q	1	47785	N/A	N/A	0.6133	hypothetical protein with esterase/lipase/thioesterase motif	scaffold_4:172513-174309		
Q	1	179141	N/A	N/A	1.1984	Fungal specific transcription factor	scaffold_4:1920533-1923036		
Q	1	39481	N/A	N/A	0.74	Aldehyde dehydrogenase	scaffold_4:2635933-2637432		
Q	1	209587	N/A	N/A	0.7678	GMC oxidoreductase	scaffold_5:1030188-1032247		
Q	1	209784	N/A	N/A	0.5586	Mitochondrial aspartate/glutamate carrier protein	scaffold_5:1752646-1754970		
Q	1	48349	N/A	N/A	1.0931	Aldo/keto reductase family proteins with RNA-binding region	scaffold_5:818287-819493		
Q	1	127635	N/A	N/A	1.0651	-	scaffold_6:1218938-1219656		
Q	1	53518	N/A	N/A	0.5203	Phosphoribosyltransferase	scaffold_6:1655229-1656096		
Q	1	48684	N/A	N/A	1.0264	(mscA) 2-methylcitrate synthase (citrate synthase family)	scaffold_6:623424-625239		
Q	1	40460	N/A	N/A	0.6098	FAD-dependent oxidoreductase	scaffold_6:634778-636119		
Q	1	56477	N/A	N/A	0.9216	Epoxide hydrolase	scaffold_7:1306445-1308023		
Q	1	53683	N/A	N/A	0.8826	-	scaffold_7:1412346-1412986		
Q	1	183268	N/A	N/A	0.4796	Hypothetical peroxisomal membrane anchor protein	scaffold_7:555335-556522		
Q	1	49420	N/A	N/A	0.4746	-	scaffold_8:1336085-1337298		
Q	1	184789	N/A	N/A	0.5644	Iron/ascorbate family oxidoreductases	scaffold_8:1619588-1620734		
Q	1	185447	N/A	N/A	0.4581	hypothetical protein with predicted Zinc finger, NF-X1-type and peptidase; KOG Class: Replication, recombination and repair; KOG Id: 1807; KOG description: Helicases	scaffold_8:552548-558493		
Q	1	185262	N/A	N/A	0.2911	Zinc-containing alcohol dehydrogenase superfamily	scaffold_8:893068-894451		
Q	1	185892	N/A	N/A	0.3925	-	scaffold_9:1559166-1561425		
Q	1	54063	N/A	N/A	0.5006	-	scaffold_9:1644656-1645915		
Q	1	42031	N/A	N/A	0.691	-	scaffold_9:21918-23352		
Q	1	56664	N/A	N/A	1.6145	Exoinulinase	scaffold_9:324573-326246		
Q	1	42152	N/A	N/A	0.7653	Esterase/lipase/thioesterase	scaffold_9:407900-409133		
Q	1	186114	N/A	N/A	0.6756	-	scaffold_9:674635-675495		
Q	1	186207	N/A	N/A	0.7728	Fungal specific transcription factor	scaffold_9:968820-971519		
Q	2	205620	N/A	N/A	0.4463	hypothetical. Interpro suggests vacuolar sorting activity	scaffold_1:1055610-1062965		
Q	2	196160	N/A	N/A	0.6397	-	scaffold_1:1146632-1148003		
Q	2	55323	N/A	N/A	0.4425	Hypothetical NADP-preferring aldehyde dehydrogenase (EC 1.2.1.5).	scaffold_1:1410834-1413001		
Q	2	122786	N/A	N/A	0.4194	Hypothetical DNA repair protein RAD1	scaffold_1:1689551-1691271		
Q	2	172413	N/A	N/A	0.8292	-	scaffold_1:1829740-1831252		
Q	2	170427	N/A	N/A	0.5845	-	scaffold_1:3801603-3802712		
Q	2	205484	N/A	N/A	0.9912	Acyl-CoA dehydrogenase	scaffold_1:545926-547462		
Q	2	187898	N/A	N/A	0.4033	Predicted glycosyltransferase	scaffold_10:1817224-1818165	139	
Q	2	202668	N/A	N/A	1.0205	Glucose/ribitol dehydrogenase	scaffold_10:1818783-1820054	139	
Q	2	211779	N/A	N/A	0.3616	Fungal specific transcription factor	scaffold_10:200904-203423	140	
Q	2	211780	N/A	N/A	0.6477	-	scaffold_10:203711-205493	140	
Q	2	188791	N/A	N/A	0.6942	Hypothetical haloacid dehalogenase-like hydrolase	scaffold_11:1610970-1611692		
Q	2	50094	N/A	N/A	0.446	NmrA-like, regulation of nitrogen utilization	scaffold_11:552334-553453		
Q	2	212771	N/A	N/A	0.4548	Zinc-binding oxidoreductase	scaffold_12:52029-53148		
Q	2	50378	N/A	N/A	0.6741	candidate β-mannanase, GH family 5 mannan endo-1,4-beta-mannosidase	scaffold_12:900158-901432		
Q	2	190654	N/A	N/A	0.6691	-	scaffold_13:144686-145804		
Q	2	54579	N/A	N/A	0.6658	Hypothetical myristoyl-CoA:protein N-myristoyltransferase	scaffold_13:556140-557815		
Q	2	126296	N/A	N/A	0.469	-	scaffold_14:679784-680739		
Q	2	51351	N/A	N/A	1.1084	Hypothetical phthalate dioxygenase reductase	scaffold_19:73166-74429		
Q	2	197860	N/A	N/A	0.5945	Hypothetical protein with RRM domain	scaffold_2:3373006-3373609		
Q	2	206489	N/A	N/A	0.3985	putative Cytochrome c oxidase, subunit VIb/COX12	scaffold_2:466992-467674		
Q	2	143583	N/A	N/A	0.7012	Hypothetical HGG motif-containing thioesterase	scaffold_2:798115-798426		
Q	2	121560	N/A	N/A	0.6997	Hypothetical ribonuclease CAF1	scaffold_20:115940-117740		
Q	2	135107	N/A	N/A	0.4681	Hypothetical Actin-binding protein	scaffold_20:125986-127141		
Q	2	176338	N/A	N/A	0.61	Hypothetical oligopeptide transporter	scaffold_3:1851870-1854344		
Q	2	176411	N/A	N/A	0.619	Haloacid dehalogenase-like hydrolase	scaffold_3:2088034-2088877		
Q	2	38275	N/A	N/A	0.8508	related to 3-ketoacyl-CoA thiolase	scaffold_3:2152405-2153839		
Q	2	37836	N/A	N/A	0.3316	-	scaffold_3:588547-589665		
Q	2	52565	N/A	N/A	0.4104	Hypothetical Vesicle coat complex COPII, subunit SEC24/subunit SFB2	scaffold_3:749662-752533		
Q	2	178353	N/A	N/A	0.436	Hypothetical N-methyltransferase	scaffold_4:2557858-2559461		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	2	52903	N/A	N/A	1.1835	-	scaffold_4:669444-670157		
Q	2	143871	N/A	N/A	0.8695	Glycoside hydrolase, starch-binding	scaffold_4:909599-909931		
Q	2	209665	N/A	N/A	0.3598	-	scaffold_5:1400994-1401969		
Q	2	53315	N/A	N/A	0.6018	related to esterase D	scaffold_5:1742933-1744109		
Q	2	199777	N/A	N/A	0.6837	Hypothetical ERG4/ERG24 ergosterol biosynthesis protein	scaffold_5:176662-180681		
Q	2	127378	N/A	N/A	0.7128	-	scaffold_5:2090464-2091131		
Q	2	56347	N/A	N/A	0.3882	Hypothetical DDHD protein	scaffold_6:1440654-1443781		
Q	2	53423	N/A	N/A	0.6664	Related to 2-methylcitrate dehydratase of E. coli	scaffold_6:586322-588188		
Q	2	49134	N/A	N/A	0.5275	Hypothetical hexokinase	scaffold_7:1446931-1448639		
Q	2	210783	N/A	N/A	0.8232	Hypothetical. Probable peroxisomal membrane. Interpro suggests alkylhydroperoxide reductase	scaffold_7:1617167-1617919		
Q	2	56498	N/A	N/A	1.2366	Isoflavone reductase	scaffold_7:1701919-1703004		
Q	2	201783	N/A	N/A	1.4638	-	scaffold_8:1588286-1589911		
Q	2	211403	N/A	N/A	0.8975	Predicted N-acetyltransferase	scaffold_9:244347-245495		
Q	3	46553	N/A	N/A	0.7501	-	scaffold_1:1835493-1836258		
Q	3	171058	N/A	N/A	0.6793	Candidate palB pH sensing peptidase	scaffold_1:2511527-2514303		
Q	3	170269	N/A	N/A	0.4867	-	scaffold_1:397197-398653		
Q	3	187802	N/A	N/A	0.5068	Hypothetical haloacid dehalogenase-like hydrolase	scaffold_10:1689001-1689786		
Q	3	190584	N/A	N/A	0.3294	-	scaffold_13:587977-589065		
Q	3	54702	N/A	N/A	0.5731	Vitamin B6 biosynthesis protein	scaffold_14:289891-290957		
Q	3	44520	N/A	N/A	0.7356	hypothetical GH family 3 β-glucosidase	scaffold_14:548320-550881		
Q	3	214233	N/A	N/A	0.4729	α-glucosidase A. Maltase glucoamylase and related hydrolases, glycosyl hydrolase family 31	scaffold_17:185513-188636		
Q	3	193828	N/A	N/A	0.2724	-	scaffold_18:184720-186980		
Q	3	214565	N/A	N/A	0.3664	Mitochondrial F1F0-ATP synthase	scaffold_18:492855-493792		
Q	3	120848	N/A	N/A	0.5128	von Willebrand factor	scaffold_2:1456342-1459158		
Q	3	206914	N/A	N/A	0.536	hypothetical protein containing basic-leucine zipper transcription factor	scaffold_2:1675610-1677475		
Q	3	206955	N/A	N/A	0.5802	Transthyretin and related proteins	scaffold_2:1788700-1789128		
Q	3	173656	N/A	N/A	1.924	Hypothetical peroxidase.	scaffold_2:2007700-2011675		
Q	3	174810	N/A	N/A	0.3427	putative extracellular protein with glycoside transferase motif	scaffold_2:2952262-2954451		
Q	3	52418	N/A	N/A	0.3596	Sugar transporter superfamily	scaffold_2:3294677-3296643		
Q	3	55178	N/A	N/A	0.514	-	scaffold_21:24878-25528		
Q	3	38023	N/A	N/A	0.5359	hypothetical Sulfite oxidase, molybdopterin-binding component	scaffold_3:1176617-1178375		
Q	3	38142	N/A	N/A	0.2426	-	scaffold_3:1709655-1712975		
Q	3	135762	N/A	N/A	0.3882	Hypothetical Molecular chaperone (small heat-shock protein Hsp26/Hsp42	scaffold_4:2528768-2529698		
Q	3	180295	N/A	N/A	1.6401	FAD-dependent oxidoreductase	scaffold_5:1127670-1129056		
Q	3	53471	N/A	N/A	0.4428	Fungal transcriptional regulatory protein	scaffold_6:1140922-1143043		
Q	3	40956	N/A	N/A	0.6556	Cytochrome P450	scaffold_7:189596-191273		
Q	3	40917	N/A	N/A	0.4876	Predicted mechanosensitive ion channel	scaffold_7:58374-60984		
Q	3	184037	N/A	N/A	0.4726	Extracellular protein with glycoside transferase motif	scaffold_7:859357-861905		
Q	3	53896	N/A	N/A	0.5298	ATP-NAD/AcoX kinase	scaffold_8:1531444-1532741		
Q	3	49747	N/A	N/A	0.8033	SWI-SNF chromatin-remodeling complex protein	scaffold_9:1524907-1527022		
Q	3	42344	N/A	N/A	0.9056	Hypothetical esterase/lipase	scaffold_9:958884-959840		
Q	4	35677	N/A	N/A	0.3219	Splicing coactivator SRm160/300, subunit SRm300	scaffold_1:1023110-1024477		
Q	4	55386	N/A	N/A	0.4964	Sulfatase	scaffold_1:2054763-2056656		
Q	4	206033	N/A	N/A	1.5974	-	scaffold_1:2341953-2343212		
Q	4	172535	N/A	N/A	0.282	Major facilitator superfamily	scaffold_1:931294-933439		
Q	4	42913	N/A	N/A	0.3253	Chitinase	scaffold_10:1137440-1139153		
Q	4	187819	N/A	N/A	0.3121	Glucose dehydrogenase/choline dehydrogenase/mandelonitrile lyase (GMC oxidoreductase family)	scaffold_10:184213-186179		
Q	4	123018	N/A	N/A	0.6356	-	scaffold_10:1889746-1891507		
Q	4	123758	N/A	N/A	0.7485	-	scaffold_10:332986-334022		
Q	4	49873	N/A	N/A	0.6757	-	scaffold_10:940700-942877		
Q	4	43217	N/A	N/A	0.3756	Major facilitator superfamily	scaffold_11:517655-519373		
Q	4	212509	N/A	N/A	0.4746	unknown, possible membrane bound	scaffold_11:570571-571985		
Q	4	212954	N/A	N/A	0.8269	-	scaffold_12:1053145-1054458		
Q	4	54707	N/A	N/A	0.6351	Involved in autophagocytosis	scaffold_14:304602-305829		
Q	4	213559	N/A	N/A	0.6382	Arginase/agmatinase/formiminoglutamase	scaffold_14:486207-487803		
Q	4	191505	N/A	N/A	0.5348	possible hexose transporter	scaffold_14:545813-547416		
Q	4	54838	N/A	N/A	0.7843	Major facilitator superfamily	scaffold_15:746859-748455		
Q	4	192202	N/A	N/A	1.0505	Transketolase, C-terminal domain	scaffold_15:755601-756827		
Q	4	44916	N/A	N/A	0.4501	candidate extracellular phospholipase C	scaffold_15:838168-839475		
Q	4	213851	N/A	N/A	0.4917	GTP cyclohydrolase II	scaffold_16:78920-83691		
Q	4	121359	N/A	N/A	0.3959	Glycosyl hydrolase family 20	scaffold_19:30669-32467		
Q	4	194584	N/A	N/A	1.044	hypothetical protein containing fungal specific transcription factor and fungal transcriptional regulatory protein domains.	scaffold_19:451396-453921		
Q	4	194594	N/A	N/A	0.8569	-	scaffold_19:581245-582019		
Q	4	173194	N/A	N/A	0.3827	Hypothetical protein. PFam indicates catechol dioxygenase activity	scaffold_2:3221169-3222222		
Q	4	207429	N/A	N/A	0.513	-	scaffold_2:3647900-3649466		
Q	4	55650	N/A	N/A	0.3626	related to 3-oxoacyl-[acyl-carrier-protein]-synthase	scaffold_2:3840913-3842700		
Q	4	46899	N/A	N/A	0.4993	-	scaffold_2:405977-407885		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	4	36722	N/A	N/A	0.4475	-	scaffold_2:505208-506429		
Q	4	176315	N/A	N/A	0.5159	Carboxymethyl transferase	scaffold_3:1755429-1756603		
Q	4	119977	N/A	N/A	0.6472	Fungal specific transcription factor	scaffold_3:2310937-2312872		
Q	4	178739	N/A	N/A	0.7617	Putative D-isomer specific 2-hydroxyacid dehydrogenase,	scaffold_4:1835181-1836320		
Q	4	39346	N/A	N/A	0.5657	hypothetical protein containing Ada, metal-binding and helix-turn-helix, AraC type domains.	scaffold_4:2229101-2229679		
Q	4	200072	N/A	N/A	0.311	Hypothetical protein with cytochrome c heme-binding site	scaffold_5:1050714-1052272		
Q	4	137541	N/A	N/A	0.462	Hypothetical mitochondrial polypeptide chain release factor	scaffold_6:457736-458231		
Q	4	134125	N/A	N/A	0.4028	Peptidase family M20/M25/M40	scaffold_6:591585-592871		
Q	4	40532	N/A	N/A	0.6182	ABC transporter	scaffold_6:841172-845939		
Q	4	184011	N/A	N/A	0.3829	Fungal specific transcription factor	scaffold_7:173948-176628		
Q	4	41120	N/A	N/A	0.5722	Predicted peptidyl-tRNA hydrolase	scaffold_7:714347-715127		
Q	4	127809	N/A	N/A	0.2846	hypothetical extracellular thaumatin domain protein	scaffold_7:731322-731756		
Q	4	41703	N/A	N/A	0.5106	GH family 88	scaffold_8:735109-736206		
Q	4	211367	N/A	N/A	0.6982	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_9:112487-113782		
Q	5	196131	N/A	N/A	0.3222	related to mitochondrial ATP synthase, subunit g	scaffold_1:1051769-1052606		
Q	5	35734	N/A	N/A	0.4484	Protein kinase	scaffold_1:1205034-1207348		
Q	5	46606	N/A	N/A	0.3321	hypothetical protein containing glycoside hydrolase, family 76 and helix-turn-helix, AraC type domains	scaffold_1:2080869-2082380		
Q	5	124797	N/A	N/A	0.7772	Major facilitator superfamily	scaffold_1:2098333-2099534		
Q	5	36075	N/A	N/A	0.8877	LeaA homologue, regulator of terrequinone A secondary metabolism	scaffold_1:2211901-2213374		
Q	5	51703	N/A	N/A	0.8966	Serine/threonine protein phosphatase	scaffold_1:228739-230427		
Q	5	46653	N/A	N/A	0.4151	-	scaffold_1:2351429-2353662		
Q	5	134276	N/A	N/A	0.6863	FOG: RRM domain	scaffold_1:2410912-2412121		
Q	5	46690	N/A	N/A	0.4393	G-protein, gamma subunit	scaffold_1:2747048-2747555		
Q	5	130394	N/A	N/A	0.2959	Flavin-containing monooxygenase	scaffold_1:330497-332236		
Q	5	187727	N/A	N/A	0.515	Hypothetical peptidase aspartic	scaffold_10:1729079-1730748		
Q	5	202682	N/A	N/A	0.4652	-	scaffold_10:1856637-1857060		
Q	5	54140	N/A	N/A	0.5683	Hypothetical myosin assembly protein/sexual cycle protein in A. niger	scaffold_10:720314-722947		
Q	5	187254	N/A	N/A	0.6528	-	scaffold_10:804630-805496		
Q	5	187103	N/A	N/A	0.5693	-	scaffold_10:993050-993678		
Q	5	56914	N/A	N/A	0.6274	Hypothetical protein with Zn-finger, C2H2 type	scaffold_11:687675-689539		
Q	5	120053	N/A	N/A	0.9266	Fungal specific transcription factor	scaffold_13:1041557-1043841		
Q	5	44193	N/A	N/A	1.1672	hypothetical carboxylesterase	scaffold_13:638962-640785		
Q	5	45333	N/A	N/A	0.3628	hypothetical zinc finger protein, C2H2 type	scaffold_17:280817-282198		
Q	5	51156	N/A	N/A	0.8702	-	scaffold_17:288190-290373		
Q	5	193610	N/A	N/A	0.4435	Carboxylesterases	scaffold_18:113953-115688		
Q	5	57403	N/A	N/A	0.4953	-	scaffold_18:419926-421424		
Q	5	45817	N/A	N/A	0.3915	β-1,6-N-acetylglucosaminyltransferase, contains WSC domain	scaffold_19:551826-553092		
Q	5	172955	N/A	N/A	0.6205	Hydantoinase/oxoprolinase	scaffold_2:100114-103181		
Q	5	131595	N/A	N/A	0.3772	Amino acid/polyamine transporter I	scaffold_2:1483425-1485165		
Q	5	138792	N/A	N/A	0.499	Alanine dehydrogenase/PNT, N-terminal	scaffold_2:2795095-2798929		
Q	5	47113	N/A	N/A	0.3787	Protein kinase	scaffold_2:3020689-3031628		
Q	5	36773	N/A	N/A	0.4981	Hypothetical enoyl-CoA hydratase. (EC 4.2.1.17) HMM predicts secretion.	scaffold_2:733019-734118		
Q	5	52169	N/A	N/A	0.4928	Hypothetical ubiquitin ligase	scaffold_2:776094-776818		
Q	5	36830	N/A	N/A	0.5192	-	scaffold_2:927461-927960		
Q	5	45912	N/A	N/A	0.6996	FMN-dependent α-hydroxy acid dehydrogenase	scaffold_20:238553-240256		
Q	5	195172	N/A	N/A	0.3729	hypothetical. N-acetyltransferase activity	scaffold_22:82679-83357		
Q	5	55721	N/A	N/A	0.6729	Sulfatase	scaffold_3:1168689-1170500		
Q	5	207831	N/A	N/A	0.6766	Glucose-methanol-choline oxidoreductase	scaffold_3:1480160-1482059		
Q	5	177912	N/A	N/A	0.4313	Protein kinase	scaffold_3:1859665-1861127		
Q	5	207572	N/A	N/A	0.5278	General substrate transporter	scaffold_3:299873-301960		
Q	5	38529	N/A	N/A	1.231	-	scaffold_3:3160860-3161994		
Q	5	38583	N/A	N/A	0.4698	-	scaffold_3:3319923-3321694		
Q	5	119438	N/A	N/A	0.5812	Phosphoprotein involved in cytosol to vacuolar targeting and autophagocytosis	scaffold_4:1219825-1222860		
Q	5	208631	N/A	N/A	0.7976	Predicted pyroglutamyl peptidase	scaffold_4:513845-514722		
Q	5	38851	N/A	N/A	1.072	homogentisate 1,2-dioxygenase	scaffold_4:578048-579599		
Q	5	55964	N/A	N/A	1.0028	Related to alcohol dehydrogenase	scaffold_4:861865-863443		
Q	5	209272	N/A	N/A	0.4205	Major facilitator superfamily	scaffold_5:127613-129012		
Q	5	209514	N/A	N/A	0.5406	Myb, DNA-binding	scaffold_5:795315-796376		
Q	5	56180	N/A	N/A	0.49	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_5:875469-877153		
Q	5	210291	N/A	N/A	0.5064	-	scaffold_6:1528947-1529666	141	
Q	5	210297	N/A	N/A	0.4276	Signal transduction	scaffold_6:1534491-1535885	141	
Q	5	53541	N/A	N/A	1.4067	-	scaffold_6:1828852-1830762		
Q	5	183143	N/A	N/A	0.4038	-	scaffold_6:241200-242549		
Q	5	181743	N/A	N/A	1.0648	hypothetical short chain dehydrogenase	scaffold_6:601088-602104		
Q	5	121960	N/A	N/A	0.7513	Predicted E3 ubiquitin ligase	scaffold_7:218211-219921		
Q	5	40967	N/A	N/A	0.3698	Related to protein kinase NPKA (Emericella nidulans)	scaffold_7:230365-231931		
Q	5	41809	N/A	N/A	0.639	Major facilitator superfamily	scaffold_8:1065214-1066885		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	5	185461	N/A	N/A	0.7296	-	scaffold_8:1333457-1334243		
Q	5	56628	N/A	N/A	0.8214	Dak kinase	scaffold_8:1544562-1546650		
Q	5	41507	N/A	N/A	0.576	hypothetical protein; KOG Class: Chromatin structure and dynamics; KOG Id: 2416; KOG description:Acinus (induces apoptotic chromatin condensation)	scaffold_8:181938-183268		
Q	5	56645	N/A	N/A	0.3929	Predicted hydrolase related to dienelactone hydrolase	scaffold_9:128926-129859		
Q	5	119127	N/A	N/A	0.814	Putatively involved in growth development in niger	scaffold_9:1473568-1477235		
Q	5	127331	N/A	N/A	0.3263	Ras small GTPase, Ras type	scaffold_9:1563924-1564713		
Q	5	42088	N/A	N/A	0.3348	-	scaffold_9:190848-193619		
Q	5	42199	N/A	N/A	0.3143	Fungal specific transcription factor	scaffold_9:532658-535407		
Q	6	121995	N/A	N/A	0.7453	-	scaffold_1:1273136-1274774		
Q	6	55366	N/A	N/A	0.3839	-	scaffold_1:1852199-1852657		
Q	6	46852	N/A	N/A	0.3592	Tyrosine specific protein phosphatase	scaffold_1:3731046-3733545		
Q	6	130150	N/A	N/A	0.4649	Serine/threonine protein kinase	scaffold_10:1037888-1041654		
Q	6	56776	N/A	N/A	0.8041	Predicted NAD-dependent oxidoreductase	scaffold_10:736651-737903		
Q	6	42825	N/A	N/A	0.3035	Protein kinase	scaffold_10:833527-836609		
Q	6	212500	N/A	N/A	1.099	Aromatic amino acid aminotransferase and related proteins	scaffold_11:514366-516323		
Q	6	50151	N/A	N/A	1.1101	hypothetical Glutathione-dependent formaldehyde-activating, GFA	scaffold_11:885919-886459		
Q	6	213042	N/A	N/A	0.6128	MOSC N-terminal β barrel domain	scaffold_13:225337-227888		
Q	6	44497	N/A	N/A	0.7593	Hypothetical mitochondrial carrier protein	scaffold_14:472641-474014		
Q	6	45801	N/A	N/A	0.9539	endo-1,6-beta-D-glucanase	scaffold_19:501123-502651		
Q	6	52410	N/A	N/A	0.5071	Hypothetical protein containing fungal specific transcription factor domain.	scaffold_2:3216720-3219917		
Q	6	38479	N/A	N/A	0.3271	Conserved hypothetical ATP binding protein	scaffold_3:2964894-2965772		
Q	6	177349	N/A	N/A	0.3157	Hypothetical Phox-like protein with Ankyrin domain	scaffold_3:3223275-3227311		
Q	6	52987	N/A	N/A	0.7665	-	scaffold_4:1570359-1570990		
Q	6	208958	N/A	N/A	0.8455	related to bZIP transcription factor AP-1	scaffold_4:2057989-2059894		
Q	6	182383	N/A	N/A	0.4375	-	scaffold_6:1632704-1633653		
Q	6	53690	N/A	N/A	0.4118	Actin-related protein Arp2/3 complex, subunit ARPC3	scaffold_7:1457701-1458688		
Q	6	48905	N/A	N/A	0.5192	Hypothetical biotin holocarboxylase synthetase/biotin-protein ligase	scaffold_7:54255-56566		
Q	6	41927	N/A	N/A	0.4554	Related to chorismate mutase of Rosellinia	scaffold_8:1434049-1435132		
Q	6	121537	N/A	N/A	0.5932	-	scaffold_9:218805-220777		
Q	6	185699	N/A	N/A	0.5331	Major facilitator superfamily	scaffold_9:633404-635121		
Q	7	51819	N/A	N/A	0.3379	Hypothetical threonyl-tRNA synthetase kinase. HMMPfam indicates Threonyl-tRNA synthetase kinase activity	scaffold_1:1350518-1352957		
Q	7	55348	N/A	N/A	1.0579	hypothetical ubiquitin-specific protease	scaffold_1:1632355-1634670		
Q	7	170479	N/A	N/A	0.4464	-	scaffold_1:1906975-1908841		
Q	7	52003	N/A	N/A	0.3513	Oxidoreductase FAD-binding domain	scaffold_1:2972047-2973235		
Q	7	206228	N/A	N/A	1.0679	Hypothetical Molecular chaperone (DnaJ superfamily	scaffold_1:3046661-3048279		
Q	7	46759	N/A	N/A	0.4668	Hypothetical protein.	scaffold_1:3108429-3112174	142	
Q	7	172476	N/A	N/A	0.5438	hypothetical protein containing fungal specific transcription factor domain.	scaffold_1:3116919-3119128	142	
Q	7	46289	N/A	N/A	0.8641	-	scaffold_1:366462-367247		
Q	7	205513	N/A	N/A	0.526	Hypothetical tri-functional histidine biosynthetic protein	scaffold_1:638906-641609		
Q	7	211909	N/A	N/A	0.7409	Hypothetical porphobilinogen deaminase	scaffold_10:673599-674669		
Q	7	50166	N/A	N/A	0.5782	Hypothetical glutathione synthase (EC 6.3.2.3). Shows some similarities with S. pombe glutathione synthase	scaffold_11:1026591-1028265		
Q	7	54354	N/A	N/A	0.595	Deduced amino acid sequence shares identity with the Saccharomyces cerevisiae NFS1 gene product; a cysteine desulfurase involved in iron-sulfur cluster (Fe/S) biogenesis; required for the post-transcriptional thio-modification of mitochondrial and cytoplasmic tRNAs.	scaffold_11:735045-736826		
Q	7	212593	N/A	N/A	0.7847	-	scaffold_11:874183-876097		
Q	7	190193	N/A	N/A	0.5244	hypothetical protein containing basic-leucine zipper transcription factor domain	scaffold_13:1018852-1020414		
Q	7	213047	N/A	N/A	0.4146	Predicted E3 ubiquitin ligase containing RING finger, subunit of transcription/repair factor TFIIH and CDK-activating kinase assembly factor	scaffold_13:251370-252480		
Q	7	44288	N/A	N/A	0.5604	Predicted panthothenate kinase/uridine kinase-related protein	scaffold_13:938046-938837		
Q	7	57150	N/A	N/A	0.8345	Hypothetical G-protein with WD-40 repeat	scaffold_14:350665-353173		
Q	7	120859	N/A	N/A	0.6467	-	scaffold_14:386945-388441		
Q	7	51125	N/A	N/A	0.855	-	scaffold_17:114529-115287		
Q	7	193467	N/A	N/A	0.5801	Cytochrome c heme-binding site	scaffold_17:270115-271940		
Q	7	54960	N/A	N/A	0.6842	Hypothetical Cyclin D-interacting protein GCIP	scaffold_17:84588-85623		
Q	7	55102	N/A	N/A	1.2097	hypothetical β-lactamase	scaffold_18:626904-628583		
Q	7	205050	N/A	N/A	0.4428	Hypothetical thioredoxin-related	scaffold_19:25515-26039		
Q	7	51373	N/A	N/A	0.6829	-	scaffold_19:377971-378832		
Q	7	127901	N/A	N/A	0.4689	-	scaffold_2:2667661-2668008		
Q	7	129843	N/A	N/A	0.4427	-	scaffold_2:2820503-2823082		
Q	7	52416	N/A	N/A	0.509	-	scaffold_2:3266094-3267147		
Q	7	52431	N/A	N/A	0.4181	putative Translation initiation factor 2, β subunit (eIF-2beta) Translation, ribosomal structure and biogenesis	scaffold_2:3382555-3384435		
Q	7	207513	N/A	N/A	0.4349	Fungal transcriptional regulatory protein	scaffold_2:3904414-3906635		
Q	7	175373	N/A	N/A	1.3295	-	scaffold_2:3960296-3961727		
Q	7	52755	N/A	N/A	0.6264	Hypothetical diacylglycerol kinase	scaffold_3:2841645-2843241		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	7	47636	N/A	N/A	0.4908	Hypothetical transcription factor TMF, TATA element modulatory factor	scaffold_3:2948753-2951462		
Q	7	39358	N/A	N/A	0.4918	Fungal specific transcription factor	scaffold_4:2260246-2262536		
Q	7	48103	N/A	N/A	1.3302	WD40 repeat-containing protein	scaffold_4:2404736-2407142		
Q	7	179814	N/A	N/A	0.5238	Phosphoserine phosphatase	scaffold_4:2510974-2512514		
Q	7	208639	N/A	N/A	0.9846	Predicted integral membrane protein	scaffold_4:533703-535590		
Q	7	180050	N/A	N/A	0.367	Predicted α/β hydrolase	scaffold_5:1152939-1154069		
Q	7	209276	N/A	N/A	0.6664	-	scaffold_5:135397-141138		
Q	7	56225	N/A	N/A	0.587	Short-chain dehydrogenase/reductase (glucose/ribitol)	scaffold_5:1631526-1632527		
Q	7	53229	N/A	N/A	0.5438	Fungal specific transcription factor	scaffold_5:878443-881490		
Q	7	48831	N/A	N/A	0.4375	-	scaffold_6:1561754-1562944		
Q	7	53510	N/A	N/A	0.794	Predicted ATPase, nucleotide-binding	scaffold_6:1581522-1582617		
Q	7	56366	N/A	N/A	0.4206	Fungal transcriptional regulatory protein	scaffold_6:1646103-1648244		
Q	7	40514	N/A	N/A	0.6755	Major facilitator superfamily	scaffold_6:778430-779857		
Q	7	53688	N/A	N/A	1.0606	Zinc-binding oxidoreductase	scaffold_7:1444839-1446123		
Q	7	184233	N/A	N/A	0.3629	Amino acid/polyamine transporter	scaffold_7:1721590-1723300		
Q	7	128352	N/A	N/A	1.1934	-	scaffold_7:640675-641032		
Q	7	53653	N/A	N/A	0.864	Beta-tubulin folding cofactor C	scaffold_7:930985-932382		
Q	7	211137	N/A	N/A	0.7852	GHMP kinase	scaffold_8:1011745-1013249		
Q	7	211330	N/A	N/A	0.5075	WD40 repeat-containing protein	scaffold_8:1647538-1650809		
Q	7	49222	N/A	N/A	0.4527	Hypothetical inositol monophosphatase	scaffold_8:187220-188278		
Q	7	56528	N/A	N/A	0.6603	Hypothetical histidinol phosphatase. HMMPfam indicates this activity. No homology to confirmed histidinol phosphatases was found	scaffold_8:238640-239634		
Q	7	120873	N/A	N/A	0.3369	Sec1-like protein	scaffold_8:973598-975475		
Q	7	46227	N/A	N/A	0.5953	-	scaffold_870:13-866		
Q	7	128428	N/A	N/A	0.4947	-	scaffold_9:1368762-1369311		
Q	8	55419	N/A	N/A	0.868	Hypothetical glycosyl hydrolase (GH family 31)	scaffold_1:2456429-2458470		
Q	8	51962	N/A	N/A	1.1823	Transcription factor, Myb superfamily	scaffold_1:2470451-2471380		
Q	8	36176	N/A	N/A	0.4827	Hypothetical 3'5'-cyclic nucleotide phosphodiesterase	scaffold_1:2741655-2744714		
Q	8	205466	N/A	N/A	0.3529	Hypothetical protein with gelsolin repeat domain	scaffold_1:503683-510673		
Q	8	205576	N/A	N/A	0.3922	hypothetical. Interpro suggests RNA-binding	scaffold_1:841304-843107		
Q	8	170624	N/A	N/A	0.3926	related to Zn-finger protein, C2H2 type domain	scaffold_1:98913-101306		
Q	8	212204	N/A	N/A	0.5882	Protein kinase	scaffold_10:1793006-1796756		
Q	8	126382	N/A	N/A	0.3337	oxidoreductase, Short-chain dehydrogenase/reductase	scaffold_10:47694-48565		
Q	8	133108	N/A	N/A	0.3475	Hypothetical phospholipid scramblase	scaffold_11:255584-257238		
Q	8	43163	N/A	N/A	0.5753	Zn-finger-like, PHD finger	scaffold_11:321072-326521		
Q	8	43968	N/A	N/A	0.3341	-	scaffold_12:1215266-1215763		
Q	8	213360	N/A	N/A	0.8714	Basic-leucine zipper (bZIP) transcription factor	scaffold_13:1120927-1121760		
Q	8	127932	N/A	N/A	0.5065	-	scaffold_13:296325-296828		
Q	8	44186	N/A	N/A	0.4429	Hypothetical protein. HMMPfam predicts short-chain dehydrogenase/reductase activity, but no similarity to proteins with confirmed activities are found. Signalp predicts secretion.	scaffold_13:623023-624158		
Q	8	129585	N/A	N/A	0.4962	RhoGEF GTPases	scaffold_17:606956-609894		
Q	8	129172	N/A	N/A	0.5423	Fungal specific transcription factor	scaffold_18:227721-231669		
Q	8	193620	N/A	N/A	0.5303	Major facilitator superfamily	scaffold_18:309700-311539		
Q	8	175389	N/A	N/A	0.5502	-	scaffold_2:3382141-3382556		
Q	8	37522	N/A	N/A	0.4197	Fungal specific transcription factor	scaffold_2:3600830-3603104		
Q	8	197039	N/A	N/A	0.639	Related to Medusa A	scaffold_2:557004-558902		
Q	8	129033	N/A	N/A	0.4785	Transcription factor MEIS1 and related HOX domain proteins	scaffold_21:97787-102205		
Q	8	52721	N/A	N/A	0.6521	-	scaffold_3:2609310-2610194		
Q	8	178699	N/A	N/A	0.6226	hypothetical BTB/POZ protein	scaffold_4:1210163-1215207		
Q	8	48042	N/A	N/A	0.7655	-	scaffold_4:1778397-1779255		
Q	8	39258	N/A	N/A	0.4073	Phenazine biosynthesis PhzC/PhzF protein	scaffold_4:1926567-1927547		
Q	8	199208	N/A	N/A	0.5433	Hypothetical cysteine peptidase, calpain like	scaffold_4:822562-825239		
Q	8	178436	N/A	N/A	0.7146	Cytochrome P450	scaffold_4:832666-834419		
Q	8	128739	N/A	N/A	0.4277	Hypothetical. RNA binding motif	scaffold_5:1223415-1229734		
Q	8	180928	N/A	N/A	0.6609	-	scaffold_5:1286087-1287745		
Q	8	181701	N/A	N/A	0.4236	Esterase/lipase/thioesterase	scaffold_5:1877375-1881069		
Q	8	125824	N/A	N/A	0.4698	Short-chain dehydrogenase/reductase	scaffold_5:2291758-2292537		
Q	8	181819	N/A	N/A	0.6397	Fungal transcriptional regulatory protein	scaffold_6:1776017-1778043		
Q	8	182206	N/A	N/A	0.6054	Isocitrate lyase	scaffold_6:1937919-1938942		
Q	8	53401	N/A	N/A	0.4481	-	scaffold_6:269120-270648		
Q	8	40469	N/A	N/A	0.6828	Fungal specific transcription factor	scaffold_6:657149-659189		
Q	8	49304	N/A	N/A	1.2727	-	scaffold_8:672614-673579		
Q	8	211376	N/A	N/A	0.575	Predicted permease for cytosine/purines, uracil, thiamine, allantoin	scaffold_9:165640-167332		
Q	8	53960	N/A	N/A	0.6266	Hypothetical DNA repair protein	scaffold_9:396750-400085		
Q	8	186748	N/A	N/A	0.4735	-	scaffold_9:723616-724878		
Q	9	170152	N/A	N/A	0.3182	Zinc-containing alcohol dehydrogenase superfamily	scaffold_1:129476-130705		
Q	9	36158	N/A	N/A	1.1866	Predicted mitochondrial carrier protein	scaffold_1:2509481-2510665		
Q	9	206308	N/A	N/A	0.3678	Hypothetical molybdenum cofactor biosynthesis protein	scaffold_1:3278822-3280040		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	9	46835	N/A	N/A	0.7511	Flavonol reductase/cinnamoyl-CoA reductase	scaffold_1:3608209-3609241		
Q	9	50019	N/A	N/A	0.3475	-	scaffold_11:149771-151501		
Q	9	212567	N/A	N/A	1.0007	Hypothetical aldo/keto reductase	scaffold_11:776121-777230		
Q	9	188691	N/A	N/A	0.3741	Hypothetical protein of the glyoxalase family	scaffold_11:941113-941720		
Q	9	138531	N/A	N/A	0.9048	-	scaffold_1194:890-1069		
Q	9	203198	N/A	N/A	1.3712	(xdhA) D-xylulose reductase	scaffold_12:15113-16374		
Q	9	190556	N/A	N/A	0.4595	DEAD/DEAH box helicase	scaffold_13:218171-220712		
Q	9	54575	N/A	N/A	0.307	Hypothetical ribosomal protein L36	scaffold_13:537196-537722		
Q	9	213288	N/A	N/A	0.6393	-	scaffold_13:888866-889385		
Q	9	54712	N/A	N/A	0.8003	Nucleoside diphosphate-sugar hydrolase of the MutT (NUDIX) family	scaffold_14:331368-332354		
Q	9	45383	N/A	N/A	0.4165	-	scaffold_17:464806-465790		
Q	9	214441	N/A	N/A	0.5088	hypothetical. KOG: acetyl-CoA acetyltransferase	scaffold_18:35959-37454		
Q	9	175251	N/A	N/A	0.8283	Hypothetical 3-hydroxyacyl-CoA dehydrogenase	scaffold_2:1065794-1066792		
Q	9	52211	N/A	N/A	0.5289	Hypothetical hydrolase related to dienelactone hydrolase	scaffold_2:1181505-1182367		
Q	9	52305	N/A	N/A	0.6871	Hypothetical homoserine dehydrogenase	scaffold_2:1867937-1869169		
Q	9	207217	N/A	N/A	1.013	glycogen synthase	scaffold_2:2943587-2945921		
Q	9	37575	N/A	N/A	0.5542	Hypothetical peptidase C12, ubiquitin carboxyl-terminal hydrolase	scaffold_2:3758925-3759758		
Q	9	130415	N/A	N/A	0.5695	Hypothetical FAD dependent oxidoreductase	scaffold_2:910802-912364		
Q	9	207936	N/A	N/A	0.5925	D-isomer specific 2-hydroxyacid dehydrogenase	scaffold_3:1850362-1851460		
Q	9	55759	N/A	N/A	0.8641	-	scaffold_3:1918850-1919976		
Q	9	175633	N/A	N/A	0.9312	Cytochrome P450	scaffold_3:2341929-2343380		
Q	9	55847	N/A	N/A	0.5877	hypothetical V-ATP synthase	scaffold_3:2951981-2953543		
Q	9	177198	N/A	N/A	0.62	-	scaffold_3:3407999-3408745		
Q	9	48803	N/A	N/A	0.7338	-	scaffold_6:1435106-1436003		
Q	9	209924	N/A	N/A	0.9814	Purine phosphorylase, family 2	scaffold_6:9543-10871		
Q	9	211162	N/A	N/A	1.0961	Hypothetical 1,4-alpha-glucan branching enzyme	scaffold_8:1046073-1048552		
Q	9	56602	N/A	N/A	0.5262	tpiA, Triosephosphate isomerase; EC 5.3.1.1; catalyzes conversion of D-glyceraldehyde 3-phosphate to glycerone phosphate in glycolysis	scaffold_8:1199508-1200655		
Q	9	185495	N/A	N/A	0.8722	endoribonuclease	scaffold_8:224044-224567		
Q	9	211731	N/A	N/A	0.6845	Peptidase M24	scaffold_9:1640106-1641650		
Q	10	35736	N/A	N/A	0.4026	mRNA cleavage and polyadenylation factor II complex	scaffold_1:1212932-1216090		
Q	10	51888	N/A	N/A	0.5525	hypothetical protein with predicted Fis and TPR; KOG Class: Chromatin structure and dynamics; KOG Id: 1156; KOG description: N-terminal acetyltransferase	scaffold_1:1913502-1916133		
Q	10	205894	N/A	N/A	0.6367	Hypothetical protein with Zn finger domain	scaffold_1:1957862-1958807		
Q	10	206081	N/A	N/A	0.7464	(topA) Topoisomerase I	scaffold_1:2524382-2527491		
Q	10	196651	N/A	N/A	0.9796	-	scaffold_1:2871135-2873655		
Q	10	206184	N/A	N/A	0.3923	-	scaffold_1:2953131-2954332		
Q	10	55240	N/A	N/A	0.6729	-	scaffold_1:350473-351372		
Q	10	51734	N/A	N/A	1.1702	GTP-binding ADP-ribosylation factor-like protein ARL2	scaffold_1:500907-501801		
Q	10	202631	N/A	N/A	0.6142	-	scaffold_10:1741741-1743020		
Q	10	132771	N/A	N/A	0.3584	Seems to be two joined proteins, a heat shock protein-like N-terminal and a phosphomannomutase	scaffold_10:1922802-1925139		
Q	10	54258	N/A	N/A	0.5208	-	scaffold_10:1952590-1953495		
Q	10	202763	N/A	N/A	0.7936	Small nuclear ribonucleoprotein	scaffold_10:2001881-2002264		
Q	10	54071	N/A	N/A	0.5824	-	scaffold_10:38164-39677		
Q	10	212624	N/A	N/A	0.4139	-	scaffold_11:1024195-1026089		
Q	10	43374	N/A	N/A	0.5324	-	scaffold_11:1073041-1074077		
Q	10	188125	N/A	N/A	0.4917	-	scaffold_11:763825-764936		
Q	10	43699	N/A	N/A	0.2972	Hypothetical kinesin-like protein	scaffold_12:417110-420718		
Q	10	54674	N/A	N/A	0.4512	candidate NADH-ubiquinone oxidoreductase subunit	scaffold_13:1206065-1206920		
Q	10	143897	N/A	N/A	0.5666	-	scaffold_14:2421-2675		
Q	10	191282	N/A	N/A	0.4917	YjeF-related protein,	scaffold_14:353470-354414		
Q	10	51019	N/A	N/A	0.7087	putative GTP binding protein	scaffold_16:517076-518726		
Q	10	54933	N/A	N/A	0.7754	Hypothetical signal peptidase	scaffold_16:844311-844936		
Q	10	214129	N/A	N/A	0.8504	Transcription factor of the Forkhead/HNF3 family	scaffold_16:880169-882319		
Q	10	204582	N/A	N/A	0.5573	-	scaffold_16:906389-906607		
Q	10	57312	N/A	N/A	0.4962	Related to C. albicans seryl-tRNA synthase (EC 6.1.1.11)	scaffold_16:912403-914213		
Q	10	204597	N/A	N/A	0.6557	Uncharacterized Zn ribbon-containing protein	scaffold_16:921343-921793		
Q	10	193484	N/A	N/A	0.4943	Hypothetical protein kinase	scaffold_17:117142-119277		
Q	10	193498	N/A	N/A	0.466	Hypothetical SNARE protein TLG2/Syntaxin 16	scaffold_17:136049-137414	143	
Q	10	135687	N/A	N/A	0.8707	-	scaffold_17:140831-141826	143	
Q	10	120292	N/A	N/A	0.6408	Fungal specific transcription factor	scaffold_17:379572-381160		
Q	10	127247	N/A	N/A	0.9344	COP9 signalosome, subunit	scaffold_18:200069-200840		
Q	10	120659	N/A	N/A	0.3588	Hypothetical protein with PPR repeat	scaffold_2:1058495-1060631		
Q	10	174765	N/A	N/A	0.712	-	scaffold_2:1377547-1380826		
Q	10	174055	N/A	N/A	0.5973	putative tRNA acetyltransferase,	scaffold_2:1704009-1705254		
Q	10	174046	N/A	N/A	0.5312	Hypothetical NADH-ubiquinone oxidoreductase	scaffold_2:2779257-2779718		
Q	10	37531	N/A	N/A	0.5421	-	scaffold_2:3627083-3628684		
Q	10	174022	N/A	N/A	0.6751	-	scaffold_2:3736518-3737537		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	10	173949	N/A	N/A	0.5087	-	scaffold_2:653064-654998		
Q	10	36764	N/A	N/A	0.6046	Hypothetical 5'-phosphoribosylglycinamide formyltransferase	scaffold_2:705508-709960		
Q	10	205236	N/A	N/A	0.4409	-	scaffold_20:321919-322509		
Q	10	138440	N/A	N/A	0.7127	-	scaffold_227:240-562		
Q	10	137267	N/A	N/A	0.5139	Hypothetical DnaJ domain protein	scaffold_3:1586760-1587527		
Q	10	208382	N/A	N/A	0.4411	Predicted GTP-binding protein (ODN superfamily)	scaffold_3:3237764-3239404		
Q	10	137661	N/A	N/A	0.5334	-	scaffold_3:3416589-3417182		
Q	10	37930	N/A	N/A	0.6118	Cytochrome P450	scaffold_3:896405-898583		
Q	10	39417	N/A	N/A	0.6035	-	scaffold_4:2447777-2449071		
Q	10	56101	N/A	N/A	0.3045	Related to dihydrolipoamide succinyltransferase (EC 2.3.1.61). May only be a subunit of the complex	scaffold_4:2919189-2921242		
Q	10	179634	N/A	N/A	0.7301	Cytochrome P450	scaffold_4:416256-417993		
Q	10	208663	N/A	N/A	1.004	-	scaffold_4:583714-586271		
Q	10	119921	N/A	N/A	0.6854	Hypothetical myosin heavy chain	scaffold_5:79993-82211		
Q	10	182731	N/A	N/A	0.3318	Zinc-containing alcohol dehydrogenase superfamily	scaffold_6:1571753-1573322		
Q	10	41442	N/A	N/A	0.5466	Zinc-containing alcohol dehydrogenase superfamily	scaffold_7:1780574-1781578		
Q	10	40970	N/A	N/A	0.4655	-	scaffold_7:237389-238512		
Q	10	48970	N/A	N/A	0.6841	-	scaffold_7:425201-426236		
Q	10	183926	N/A	N/A	0.7485	hypothetical class II aldolase/adducin domain protein	scaffold_7:704789-705961		
Q	10	210651	N/A	N/A	0.5122	AAA ATPase	scaffold_7:812169-813670		
Q	10	53870	N/A	N/A	0.918	-	scaffold_8:1238393-1241137		
Q	10	41494	N/A	N/A	0.3783	-	scaffold_8:129615-130850		
Q	10	184532	N/A	N/A	0.8153	Hypothetical hydroxyacylglutathione hydrolase	scaffold_8:1514067-1515300		
Q	10	53811	N/A	N/A	0.2805	Related to profilin an actin bindin protein involved in cytoskeleton dynamics	scaffold_8:814548-815302		
Q	10	186766	N/A	N/A	1.0735	-	scaffold_9:1148665-1149246		
Q	10	54041	N/A	N/A	1.039	Tubulin binding cofactor A	scaffold_9:1416582-1417079		
Q	10	185842	N/A	N/A	0.8564	cytochrome b5	scaffold_9:1581809-1582239		
Q	10	186329	N/A	N/A	0.3426	Hypothetical P-type ATPase	scaffold_9:206084-210802		
Q	10	201896	N/A	N/A	0.6837	Hypothetical Ubiquitin-specific protease	scaffold_9:307320-309052		
Q	11	134002	N/A	N/A	0.626	Major facilitator superfamily	scaffold_1:1838255-1839858		
Q	11	51881	N/A	N/A	0.3897	Deduced protein shares amino acid sequence identity with the Saccharomyces cerevisiae RSA4 gene product; a WD-repeat protein involved in ribosome biogenesis; required for maturation and efficient intra-nuclear transport or pre-60S ribosomal subunits, localizes to the nucleolus.	scaffold_1:1861279-1862562		
Q	11	35440	N/A	N/A	0.4605	Hypothetical phosphatidylserine decarboxylase (EC 4.1.1.65)	scaffold_1:236779-238419		
Q	11	205494	N/A	N/A	0.5177	B-cell receptor-associated protein and related proteins	scaffold_1:578934-579840		
Q	11	203350	N/A	N/A	0.506	Hypothetical RNA splicing coactivator	scaffold_12:508992-510680		
Q	11	43788	N/A	N/A	0.3898	Hypothetical phospholipase A2	scaffold_12:668418-670157		
Q	11	44450	N/A	N/A	0.6694	-	scaffold_14:330248-331176		
Q	11	57261	N/A	N/A	0.6263	Hypothetical Chaperone DnaJ	scaffold_16:501659-502909		
Q	11	194073	N/A	N/A	0.3597	-	scaffold_18:474125-474682		
Q	11	205095	N/A	N/A	0.4735	Short-chain dehydrogenase/reductase	scaffold_19:343724-344608		
Q	11	52303	N/A	N/A	0.8177	-	scaffold_2:1856199-1857113		
Q	11	141709	N/A	N/A	0.4228	-	scaffold_2:1869264-1870519		
Q	11	52391	N/A	N/A	0.9082	-	scaffold_2:3007711-3009737		
Q	11	206461	N/A	N/A	0.456	Protein kinase	scaffold_2:341934-344060		
Q	11	194913	N/A	N/A	0.7584	Amino acid/polyamine transporter	scaffold_21:256718-258445		
Q	11	208139	N/A	N/A	0.6837	-	scaffold_3:2411757-2414020		
Q	11	38457	N/A	N/A	0.3463	V-ATPase subunit C	scaffold_3:2903825-2905226		
Q	11	176918	N/A	N/A	0.4597	-	scaffold_3:3409231-3409731		
Q	11	178864	N/A	N/A	0.4616	Protein involved in ubiquinone biosynthesis	scaffold_4:2556531-2557464		
Q	11	199203	N/A	N/A	0.4666	-	scaffold_4:802557-804004		
Q	11	53289	N/A	N/A	0.6195	-	scaffold_5:1512030-1514001		
Q	11	180255	N/A	N/A	0.5008	neutral zinc metallopeptidases	scaffold_5:2333649-2335856		
Q	11	183116	N/A	N/A	0.4723	Hypothetical leucyl-tRNA synthetase	scaffold_6:135675-138767		
Q	11	210546	N/A	N/A	0.5239	-	scaffold_7:482492-486249		
Q	11	56514	N/A	N/A	0.6468	Protein kinase	scaffold_8:70962-73151		
Q	12	51788	N/A	N/A	0.5259	hypothetical protein containing basic-leucine zipper transcription factor domain	scaffold_1:1077434-1079340		
Q	12	51812	N/A	N/A	1.7721	Hypothetical D-lactate dehydrogenase	scaffold_1:1288621-1289670		
Q	12	206203	N/A	N/A	0.8791	Zinc-containing alcohol dehydrogenase	scaffold_1:2995390-2996745		
Q	12	212182	N/A	N/A	1.3784	-	scaffold_10:1753260-1754069		
Q	12	54093	N/A	N/A	0.7007	Phosphofructokinase	scaffold_10:328819-331273		
Q	12	202464	N/A	N/A	0.7774	Aminotransferase, class-II	scaffold_10:890019-891884		
Q	12	143946	N/A	N/A	1.1777	Hypothetical, with signal sequence	scaffold_11:373452-373795		
Q	12	212788	N/A	N/A	0.5748	Calcium-responsive transcription coactivator	scaffold_12:100792-103387		
Q	12	212768	N/A	N/A	1.402	Related to malic oxidoreductase from S. cerevisiae (EC 1.1.1.40). May be the mitochondrial isoenzyme of protein 211661.	scaffold_12:48392-50565		
Q	12	143899	N/A	N/A	1.649	-	scaffold_13:1216054-1216376		
Q	12	190884	N/A	N/A	0.5359	Cys/Met metabolism pyridoxal-phosphate-dependent enzymes	scaffold_13:29126-30377		
Q	12	54686	N/A	N/A	0.6385	-	scaffold_14:139009-140952		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	12	213512	N/A	N/A	0.9052	Aldo/keto reductase family proteins	scaffold_14:340239-341172		
Q	12	213533	N/A	N/A	0.8823	-	scaffold_14:409679-412455		
Q	12	122081	N/A	N/A	0.3841	Fungal transcriptional regulatory protein	scaffold_14:663222-664844		
Q	12	44612	N/A	N/A	0.3793	Related to phenylacrylic acid decarboxylase	scaffold_14:846133-846816		
Q	12	213788	N/A	N/A	1.0081	candidate GABA permease	scaffold_15:472637-474372		
Q	12	204476	N/A	N/A	0.9266	Zinc-containing alcohol dehydrogenase	scaffold_16:682133-683293		
Q	12	121090	N/A	N/A	0.5109	Protein tyrosine phosphatase,	scaffold_2:1054091-1055795		
Q	12	206756	N/A	N/A	0.3834	Hypothetical phosphatidylinositol-4-phosphate 5-kinase	scaffold_2:1238211-1239300		
Q	12	206952	N/A	N/A	0.5299	candidate bZIP transcription factor AtfA	scaffold_2:1783322-1785360		
Q	12	36647	N/A	N/A	0.6243	Lipocalin-related protein	scaffold_2:254848-256231		
Q	12	207261	N/A	N/A	0.6018	NADH:flavin oxidoreductase/NADH oxidase	scaffold_2:3089642-3090889		
Q	12	173481	N/A	N/A	0.6315	-	scaffold_2:3592768-3595445		
Q	12	196989	N/A	N/A	0.4889	similar to the PTAB putative transcription activator of Aspergillus nidulans	scaffold_2:436312-438851		
Q	12	36820	N/A	N/A	1.7683	-	scaffold_2:887185-888017		
Q	12	214876	N/A	N/A	0.9699	-	scaffold_24:82702-83204		
Q	12	52675	N/A	N/A	2.0595	Glycosyl transferase, family 35	scaffold_3:2073447-2076571		
Q	12	176564	N/A	N/A	0.7304	-	scaffold_3:3041388-3042315		
Q	12	207595	N/A	N/A	1.039	Cytochrome P450	scaffold_3:384572-385934		
Q	12	52865	N/A	N/A	1.1198	Hypothetical, possible DNA binding	scaffold_4:279962-280695		
Q	12	200218	N/A	N/A	1.0527	-	scaffold_5:1644914-1646201		
Q	12	53210	N/A	N/A	0.674	Mitochondrial ATPase inhibitor, IATP	scaffold_5:689274-689868		
Q	12	48814	N/A	N/A	0.993	-	scaffold_6:1483903-1486792		
Q	12	124160	N/A	N/A	0.4499	Disintegrin metalloproteinases with thrombospondin repeats	scaffold_7:521067-523006		
Q	12	53645	N/A	N/A	1.1778	candidate sterol desaturase	scaffold_7:828353-829376		
Q	12	201359	N/A	N/A	1.083	-	scaffold_8:189262-190386		
Q	12	210921	N/A	N/A	0.5282	Predicted E3 ubiquitin ligase	scaffold_8:275215-277404		
Q	12	202131	N/A	N/A	1.7348	-	scaffold_9:1402625-1404918		
Q	12	42514	N/A	N/A	0.7978	-	scaffold_9:1491075-1493208		
Q	12	185790	N/A	N/A	1.1229	-	scaffold_9:757297-759018		
Q	13	205346	N/A	N/A	1.9543	-	scaffold_1:30702-32136	144	
Q	13	136667	N/A	N/A	1.2924	Cytochrome P450	scaffold_1:37064-37612	144	
Q	13	171092	N/A	N/A	0.7104	Monooxygenase involved in coenzyme Q (ubiquinone) biosynthesis	scaffold_1:845897-847882		
Q	13	56846	N/A	N/A	1.2853	-	scaffold_10:1914177-1915251		
Q	13	212003	N/A	N/A	0.8289	Hypothetical DnaJ domain protein	scaffold_10:900189-901913		
Q	13	212444	N/A	N/A	0.5979	-	scaffold_11:347141-350661		
Q	13	50105	N/A	N/A	0.6334	hypothetical glucose transporter	scaffold_11:656789-658069		
Q	13	203335	N/A	N/A	1.2903	-	scaffold_12:427599-428176		
Q	13	44893	N/A	N/A	1.3313	Putative esterase/lipase/thioesterase	scaffold_15:773052-774272		
Q	13	193120	N/A	N/A	0.423	WD40 repeat-containing protein	scaffold_17:599743-602560		
Q	13	125912	N/A	N/A	1.6448	-	scaffold_18:604927-605953		
Q	13	123955	N/A	N/A	1.5871	Predicted alcohol dehydrogenase	scaffold_19:615834-616980		
Q	13	36867	N/A	N/A	2.1551	Hypothetical Mitochondrial substrate (phosphate) carrier	scaffold_2:1076514-1077701		
Q	13	52274	N/A	N/A	0.7117	-	scaffold_2:1667017-1667838		
Q	13	52318	N/A	N/A	1.5781	Hypothetical glycosyl transferase. Related to N. crassa clock-controlled gene-9 protein	scaffold_2:1960237-1962589		
Q	13	37145	N/A	N/A	0.574	hypothetical amine oxidase	scaffold_2:2032181-2033908		
Q	13	52139	N/A	N/A	0.7467	Peripheral-type benzodiazepine receptor	scaffold_2:499296-499937		
Q	13	208152	N/A	N/A	0.3874	-	scaffold_3:2597474-2599493		
Q	13	137696	N/A	N/A	1.4145	Glutathione-dependent formaldehyde-activating,	scaffold_3:3260016-3260598		
Q	13	38647	N/A	N/A	1.3165	-	scaffold_3:3505407-3506157		
Q	13	207611	N/A	N/A	1.75	Hypothetical FAD-dependent oxidoreductase/Fumarate reductase/succinate dehydrogenase	scaffold_3:474156-475446		
Q	13	198257	N/A	N/A	1.2853	-	scaffold_3:912403-912873		
Q	13	39172	N/A	N/A	0.9999	Zinc-containing alcohol dehydrogenase	scaffold_4:1624481-1625554		
Q	13	208917	N/A	N/A	0.7968	Ubiquitin-conjugating enzyme	scaffold_4:1766067-1766636		
Q	13	208713	N/A	N/A	1.2868	-	scaffold_4:804949-806015		
Q	13	39869	N/A	N/A	1.6896	RRM domain	scaffold_5:1057459-1058080		
Q	13	53356	N/A	N/A	0.8623	Alcohol dehydrogenase involved in secondary metabolism	scaffold_5:2164124-2165348		
Q	13	39560	N/A	N/A	1.6174	-	scaffold_5:3690-4820		
Q	13	209561	N/A	N/A	0.7175	Fatty acid desaturase	scaffold_5:924283-926024		
Q	13	39844	N/A	N/A	1.1794	-	scaffold_5:977678-978507		
Q	13	40862	N/A	N/A	0.8353	hypothetical protein	scaffold_6:1914150-1914710		
Q	13	209956	N/A	N/A	0.6515	Protein kinase	scaffold_6:67031-68663		
Q	13	53549	N/A	N/A	1.2548	UDP-glucuronosyl and UDP-glucosyl transferase	scaffold_7:134399-136091		
Q	13	184005	N/A	N/A	0.8634	AKG-dependent taurine catabolism dioxygenase T	scaffold_7:1363040-1364460		
Q	13	49156	N/A	N/A	0.3868	Major facilitator superfamily	scaffold_7:1613153-1614802		
Q	13	185605	N/A	N/A	1.2069	-	scaffold_8:234204-235573		
Q	13	201412	N/A	N/A	1.3741	-	scaffold_8:303588-304264		
Q	13	42362	N/A	N/A	1.115	Major facilitator superfamily	scaffold_9:1000941-1002362		
Q	13	211476	N/A	N/A	0.3654	Fungal transcriptional regulatory protein	scaffold_9:446920-449522		

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Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	14	46243	N/A	N/A	0.85	Major facilitator superfamily	scaffold_1:32516-34482		
Q	14	206384	N/A	N/A	2.5008	related to aspartic protease	scaffold_1:3856825-3858220		
Q	14	42810	N/A	N/A	0.6207	-	scaffold_10:783432-784477		
Q	14	54387	N/A	N/A	0.4556	-	scaffold_11:1062773-1065199		
Q	14	43342	N/A	N/A	0.7667	putative transmembrane GH family 31	scaffold_11:947705-949915		
Q	14	43695	N/A	N/A	0.6205	-	scaffold_12:394400-395461		
Q	14	191345	N/A	N/A	1.4403	related to carbonic anhydrase, protection against oxidative damage	scaffold_14:153296-154060		
Q	14	213490	N/A	N/A	2.0717	-	scaffold_14:311385-312131		
Q	14	213782	N/A	N/A	0.8742	-	scaffold_15:461558-463520		
Q	14	191841	N/A	N/A	0.7016	Dehydrogenases with different specificities	scaffold_15:577146-578207		
Q	14	51124	N/A	N/A	1.7765	-	scaffold_17:112292-113406		
Q	14	193741	N/A	N/A	1.1573	-	scaffold_18:524780-525961		
Q	14	197162	N/A	N/A	0.5289	Sugar (ANd other) transporter	scaffold_2:919483-921285		
Q	14	38015	N/A	N/A	0.8149	Glycoside hydrolase, family 18	scaffold_3:1150295-1151876		
Q	14	52767	N/A	N/A	0.5136	Hypothetical transcription factor containing C2HC type Zn finger	scaffold_3:2973461-2973988		
Q	14	47934	N/A	N/A	0.8474	-	scaffold_4:1125414-1127126		
Q	14	178600	N/A	N/A	0.9374	Cytochrome c heme-binding site	scaffold_4:2150343-2150927		
Q	14	178371	N/A	N/A	0.6909	Splicing coactivator SRm160/300,	scaffold_4:2690509-2692385		
Q	14	199159	N/A	N/A	0.559	-	scaffold_4:639527-641353		
Q	14	209279	N/A	N/A	1.4951	Fructose-2,6-bisphosphatase	scaffold_5:141697-144246		
Q	14	180844	N/A	N/A	0.5729	Short-chain dehydrogenase/reductase SDR	scaffold_5:600404-601685		
Q	14	40838	N/A	N/A	0.7702	Fe2+/Zn2+ regulated transporter	scaffold_6:1821313-1822377		
Q	14	210700	N/A	N/A	1.2508	-	scaffold_7:1199305-1200702		
Q	14	184246	N/A	N/A	0.687	Hypothetical RasGAP protein	scaffold_7:667067-669494		
Q	14	41113	N/A	N/A	1.2989	-	scaffold_7:691234-691761		
Q	14	53901	N/A	N/A	0.6373	-	scaffold_8:1581861-1583558		
Q	14	210957	N/A	N/A	1.0339	-	scaffold_8:385153-386710		
Q	14	123645	N/A	N/A	0.8941	Hypothetical GCN5-related N-acetyltransferase	scaffold_8:437403-439736		
Q	14	53795	N/A	N/A	1.1562	ABC transporter	scaffold_8:663001-667820		
Q	14	49626	N/A	N/A	0.7479	-	scaffold_9:870274-871368		
Q	15	196729	N/A	N/A	0.5792	Hypothetical Cyclin-like protein	scaffold_1:3034285-3035517		
Q	15	206243	N/A	N/A	1.0457	Sodium/calcium exchanger protein	scaffold_1:3093129-3094576		
Q	15	124966	N/A	N/A	0.5883	-	scaffold_1:3517951-3519041		
Q	15	187263	N/A	N/A	0.7166	-	scaffold_10:1734714-1735931		
Q	15	42652	N/A	N/A	0.3905	Glutaredoxin	scaffold_10:267834-269469		
Q	15	43248	N/A	N/A	0.4359	-	scaffold_11:672492-673271		
Q	15	189635	N/A	N/A	1.0284	Monodehydroascorbate/ferredoxin reductase	scaffold_12:156472-158270		
Q	15	54532	N/A	N/A	0.5129	Amino acid/polyamine transporter I	scaffold_13:211729-213653		
Q	15	128900	N/A	N/A	0.3571	Predicted mitochondrial carrier protein	scaffold_2:1313606-1318310	145	
Q	15	206783	N/A	N/A	1.2987	-	scaffold_2:1321187-1323301	145	
Q	15	195147	N/A	N/A	0.4328	-	scaffold_22:51769-52446	146	
Q	15	214857	N/A	N/A	0.3282	Pectinesterase	scaffold_22:53016-54105	146	
Q	15	195339	N/A	N/A	1.2269	-	scaffold_26:4166-5207		
Q	15	198099	N/A	N/A	1.3209	Chloroperoxidase	scaffold_3:407254-408242		
Q	15	39523	N/A	N/A	0.3324	-	scaffold_4:2830914-2831875		
Q	15	48853	N/A	N/A	0.572	Hypothetical DNA-directed RNA polymerase	scaffold_6:1649481-1651325		
Q	15	183086	N/A	N/A	0.3941	-	scaffold_6:194416-195099		
Q	15	181931	N/A	N/A	0.5126	Transcription factor with Helix-loop-helix DNA-binding domain	scaffold_6:950552-951672		
Q	15	183186	N/A	N/A	0.8103	Hypothetical Isoflavone reductase	scaffold_7:1605609-1606661		
Q	15	53655	N/A	N/A	0.6729	-	scaffold_7:960651-961708		
Q	15	184754	N/A	N/A	0.2953	-	scaffold_8:1236990-1238143		
Q	16	51817	N/A	N/A	0.5184	Fungal transcriptional regulatory protein	scaffold_1:1342981-1345075		
Q	16	42613	N/A	N/A	0.3235	Esterase/lipase/thioesterase	scaffold_10:152182-152934		
Q	16	42695	N/A	N/A	0.3534	-	scaffold_10:400172-401178		
Q	16	54305	N/A	N/A	1.8849	Zinc-containing alcohol dehydrogenase	scaffold_11:222118-223732		
Q	16	50097	N/A	N/A	0.9281	-	scaffold_11:558221-559363		
Q	16	143379	N/A	N/A	0.6033	candidate mismatched base pair and cruciform DNA recognition protein	scaffold_11:740931-741508		
Q	16	50266	N/A	N/A	0.5729	helicase Swr1	scaffold_12:64999-70084		
Q	16	213350	N/A	N/A	0.7545	-	scaffold_13:1100567-1101106		
Q	16	45346	N/A	N/A	0.3601	Exocyst complex subunit	scaffold_17:339108-341381		
Q	16	57320	N/A	N/A	0.5133	Fungal specific transcription factor	scaffold_17:99822-102136		
Q	16	130357	N/A	N/A	0.4295	-	scaffold_18:188274-190911		
Q	16	125022	N/A	N/A	0.707	Predicted dehydrogenase	scaffold_19:601445-602488		
Q	16	173264	N/A	N/A	0.5788	Cytochrome c heme-binding site	scaffold_2:1753776-1757892		
Q	16	173711	N/A	N/A	0.5345	Short-chain dehydrogenase/reductase	scaffold_2:3369299-3370369		
Q	16	128147	N/A	N/A	1.7874	-	scaffold_2:3692467-3692814		
Q	16	119598	N/A	N/A	0.5306	Hypothetical protein with Zn-finger-like, PHD finger domain	scaffold_20:166468-169108		
Q	16	144007	N/A	N/A	0.8139	-	scaffold_272:951-1293		

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Continued from last page

Subset	Cluster	Gene	HiLo	MeLo	HiMe	Annotation	Location	Co-localized	Sec metabolite
Q	16	177966	N/A	N/A	0.4394	Fungal specific transcription factor	scaffold_3:1075409-1077676		
Q	16	207948	N/A	N/A	1.1267	-	scaffold_3:1874053-1874536		
Q	16	208059	N/A	N/A	0.2657	Cyclase-associated protein	scaffold_3:2120712-2122539		
Q	16	52731	N/A	N/A	0.27	Major facilitator superfamily	scaffold_3:2678543-2687638		
Q	16	38549	N/A	N/A	0.3425	-	scaffold_3:3217756-3219673		
Q	16	47268	N/A	N/A	0.7228	-	scaffold_3:527698-528456		
Q	16	144129	N/A	N/A	0.6515	-	scaffold_337:1181-1431		
Q	16	179076	N/A	N/A	0.6501	Putative transcription factor with SET domain	scaffold_4:2536538-2539266		
Q	16	181434	N/A	N/A	0.6328	Serine-threonine phosphatase 2B	scaffold_5:1622162-1624092		
Q	16	53521	N/A	N/A	0.4231	Hypothetical COP9 signalosome, subunit CSN5	scaffold_6:1679160-1679924		
Q	16	183100	N/A	N/A	0.5903	Flavoprotein monooxygenase	scaffold_6:1793430-1795624		
Q	16	182745	N/A	N/A	0.6514	Lipoprotein	scaffold_6:279286-281778		
Q	16	181901	N/A	N/A	0.4153	-	scaffold_6:906499-908345		
Q	16	41249	N/A	N/A	0.5866	Chitinase	scaffold_7:1134610-1135804		
Q	16	49061	N/A	N/A	0.5586	-	scaffold_7:831854-834816		
Q	16	41930	N/A	N/A	1.014	-	scaffold_8:1440197-1440708		
Q	16	56633	N/A	N/A	0.4347	-	scaffold_8:1632034-1632955		
Q	16	41602	N/A	N/A	0.405	Sodium/hydrogen exchanger family	scaffold_8:442642-444523		
Q	16	186313	N/A	N/A	0.5895	hypothetical nuclear.Predicted domains: SNF2-related, Helicase C-terminal, cytochrome C, Zn-finger, DEAD/DEAH box helicase and C-5 cytosine-specific DNA methylaseSNF2 family helicase	scaffold_9:1082286-1088826		
Q	16	186253	N/A	N/A	0.3536	Predicted transporter (major facilitator superfamily)	scaffold_9:1410387-1412227		
Q	17	46500	N/A	N/A	0.4908	-	scaffold_1:1523340-1524581		
Q	17	119367	N/A	N/A	0.7694	Endoplasmic reticulum protein EP58	scaffold_1:2541587-2544778		
Q	17	55432	N/A	N/A	0.8002	-	scaffold_1:2772551-2776269		
Q	17	205428	N/A	N/A	1.3926	-	scaffold_1:401114-402322		
Q	17	171242	N/A	N/A	0.7462	-	scaffold_1:443540-444911		
Q	17	140013	N/A	N/A	0.6684	Major facilitator superfamily	scaffold_10:195140-196384		
Q	17	212618	N/A	N/A	0.9953	Hypothetical carbonic anhydrase	scaffold_11:1015615-1016406		
Q	17	54414	N/A	N/A	0.5018	short chain dehydrogenase	scaffold_11:1458514-1459674		
Q	17	188160	N/A	N/A	0.4458	-	scaffold_11:966528-967918		
Q	17	189666	N/A	N/A	0.8677	Aminoacyl-tRNA synthetase	scaffold_12:998763-999148		
Q	17	44289	N/A	N/A	0.9058	-	scaffold_13:940531-941274		
Q	17	120638	N/A	N/A	0.5383	Fungal transcriptional regulatory protein	scaffold_14:51126-53525		
Q	17	141605	N/A	N/A	1.13	Putative signal transduction protein involved in RNA splicing	scaffold_15:49101-50208		
Q	17	54828	N/A	N/A	1.4836	-	scaffold_15:555443-556858		
Q	17	50950	N/A	N/A	0.347	-	scaffold_16:114318-117433		
Q	17	193556	N/A	N/A	0.4862	Predicted transporter (major facilitator superfamily)	scaffold_17:320718-322379		
Q	17	45403	N/A	N/A	0.3009	-	scaffold_17:532456-534728		
Q	17	55077	N/A	N/A	0.6385	DNA-binding protein of the nucleobindin family	scaffold_18:424957-426294		
Q	17	205005	N/A	N/A	1.171	putative soluble Fumarate reductase/succinate dehydrogenase flavoprotein, N-terminal	scaffold_18:536189-538373		
Q	17	173916	N/A	N/A	0.7018	-	scaffold_2:119871-120913		
Q	17	37009	N/A	N/A	1.1932	-	scaffold_2:1572591-1574489		
Q	17	206982	N/A	N/A	0.7435	hypothetical protein with esterase/lipase/thioesterase and signal ppetide motifs	scaffold_2:1836287-1841194		
Q	17	174255	N/A	N/A	0.3969	Hypothetical protein with Zn-finger-like, PHD finger	scaffold_2:1972434-1975141		
Q	17	174284	N/A	N/A	0.8003	-	scaffold_2:2866414-2867878		
Q	17	52153	N/A	N/A	0.5507	Hypothetical protein with KH domain	scaffold_2:630069-633398		
Q	17	45844	N/A	N/A	0.319	Oxidoreductase	scaffold_20:527-1849		
Q	17	176705	N/A	N/A	0.7314	hypothetical Histone H3 methyltransferase SUV39H1/Clr4	scaffold_3:2817770-2818975		
Q	17	141168	N/A	N/A	0.946	hypothetical protein	scaffold_3:3355869-3357169		
Q	17	37775	N/A	N/A	0.5339	hypothetical protein containing Zn-finger, C2H2 type domain	scaffold_3:398279-400807		
Q	17	176969	N/A	N/A	0.5639	putative TdiE homologue, part of LaeA regulated cluster in A. nidulans	scaffold_3:446996-447967		
Q	17	137853	N/A	N/A	0.474	-	scaffold_4:1724138-1724503		
Q	17	179788	N/A	N/A	0.3397	Hypothetical DNA-directed DNA polymerase B	scaffold_4:2439042-2444107		
Q	17	39551	N/A	N/A	1.2479	Protein-L-isoaspartate(D-aspartate) O-methyltransferase	scaffold_4:2916013-2916953		
Q	17	55971	N/A	N/A	1.5748	Alcohol dehydrogenase, class V	scaffold_4:999883-1001047		
Q	17	200307	N/A	N/A	0.5258	-	scaffold_5:1858185-1858430		
Q	17	209422	N/A	N/A	0.8312	-	scaffold_5:528242-529097		
Q	17	180171	N/A	N/A	0.5613	Hypothetical isocitrate lyase and phosphorylmutase	scaffold_5:547787-548757		
Q	17	183029	N/A	N/A	0.3261	Candidate Two-component system protein A	scaffold_6:667581-669602	147	6
Q	17	181803	N/A	N/A	0.6488	Polyketide synthase	scaffold_6:671718-680022	147	6
Q	17	40477	N/A	N/A	1.9375	Hypothetical. Some similarity to alkylhydroperoxidase	scaffold_6:684221-684949	147	6
Q	17	40478	N/A	N/A	2.1294	Aromatic-ring hydroxylase	scaffold_6:687022-688454	147	6
Q	17	41915	N/A	N/A	0.6149	-	scaffold_8:1395358-1396666		
Q	17	184665	N/A	N/A	0.4893	-	scaffold_8:88511-90145		
Q	17	49589	N/A	N/A	0.4088	-	scaffold_9:583151-584371		

F.3.3 GO-term over-representation tables

GO-term over-representation results for all clusters of table F.2 except cluster D which only has one gene. For each of the three ontologies (Metabolic function, Biological process, and Cellular component) is shown the significant (p.elim < 0.05) terms.

```
############################################
##                                        ##
##               Group A                  ##
##                                        ##
############################################

> ##########  Metabolic function  #############

    GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1  GO:0005279 amino acid-polyamine transporter activit...        87           4     0.39               1 0.00053 0.99 0.00053 0.00053
2  GO:0008471                            laccase activity         1           1     0.00               7 0.00445 1.00 0.00445 0.00445
3  GO:0004807         triose-phosphate isomerase activity         3           1     0.01               9 0.01329 1.00 0.01329 0.01329
4  GO:0008519               ammonium transporter activity         3           1     0.01              10 0.01329 1.00 0.01329 0.01329
5  GO:0008810                          cellulase activity         3           1     0.01              11 0.01329 1.00 0.01329 0.01329
6  GO:0015101         organic cation transporter activity         3           1     0.01              12 0.01329 1.00 0.01329 1.00000
7  GO:0009049     aspartic-type signal peptidase activity         4           1     0.02              13 0.01768 1.00 0.01768 0.01768
8  GO:0042499           signal peptide peptidase activity         4           1     0.02              14 0.01768 1.00 0.01768 0.01768
9  GO:0042500 aspartic endopeptidase activity, intrame...         4           1     0.02              15 0.01768 1.00 0.01768 1.00000
10 GO:0004100                    chitin synthase activity         6           1     0.03              19 0.02641 0.16 0.02641 0.02641
11 GO:0004160         dihydroxy-acid dehydratase activity         6           1     0.03              20 0.02641 0.76 0.02641 0.02641
12 GO:0008061                              chitin binding         7           1     0.03              21 0.03074 0.96 0.03074 0.03074
13 GO:0009003                  signal peptidase activity         7           1     0.03              22 0.03074 0.81 0.03074 1.00000
14 GO:0003910                  DNA ligase (ATP) activity        11           1     0.05              24 0.04790 0.47 0.04790 0.04790

> ##########  Cellular component  #############

    GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS  elim  weight
1  GO:0016020                                  membrane      1079           9     4.19               1   0.001 0.2347 0.001 0.00020

> ##########  Biological process  #############

        GO.ID                                       Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1  GO:0006865                          amino acid transport        87           4     0.34               1 0.00029 0.95 0.00029 0.00029
2  GO:0005976             polysaccharide metabolic process        17           2     0.07               5 0.00187 0.92 0.00187 1.00000
3  GO:0051340                regulation of ligase activity         3           1     0.01              10 0.01160 1.00 0.01160 0.01160
4  GO:0000272             polysaccharide catabolic process         5           1     0.02              11 0.01926 1.00 0.01926 0.01926
5  GO:0006031                  chitin biosynthetic process         5           1     0.02              12 0.01926 0.24 0.01926 0.01926
6  GO:0006042             glucosamine biosynthetic process         5           1     0.02              13 0.01926 0.24 0.01926 1.00000
7  GO:0006045    N-acetylglucosamine biosynthetic process         5           1     0.02              14 0.01926 0.24 0.01926 1.00000
8  GO:0046349             amino sugar biosynthetic process         5           1     0.02              15 0.01926 0.24 0.01926 1.00000
9  GO:0006030                    chitin metabolic process         6           1     0.02              16 0.02307 0.49 0.02307 1.00000
10 GO:0006040                amino sugar metabolic process         8           1     0.03              17 0.03065 0.51 0.03065 1.00000
11 GO:0006041                glucosamine metabolic process         8           1     0.03              18 0.03065 0.51 0.03065 1.00000
12 GO:0006044       N-acetylglucosamine metabolic process         8           1     0.03              19 0.03065 0.51 0.03065 1.00000
13 GO:0000271          polysaccharide biosynthetic process         9           1     0.03              20 0.03442 0.61 0.03442 1.00000
14 GO:0016998                  cell wall catabolic process        10           1     0.04              21 0.03818 0.16 0.03818 0.03818
15 GO:0009082 branched chain family amino acid biosynt...        12           1     0.05              22 0.04564 1.00 0.04564 0.04564
16 GO:0044264 cellular polysaccharide metabolic proces...        12           1     0.05              23 0.04564 0.52 0.04564 1.00000
```

```
##############################################
##                                          ##
##                Group B                   ##
##                                          ##
##############################################

> ##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS   elim weight
1  GO:0004466 long-chain-acyl-CoA dehydrogenase activi...         1           1     0.01               1  0.0084 1.000 0.0084 0.0084
2  GO:0008898 homocysteine S-methyltransferase activit...         1           1     0.01               2  0.0084 1.000 0.0084 0.0084
3  GO:0017039           dipeptidyl-peptidase III activity         1           1     0.01               3  0.0084 1.000 0.0084 0.0084
4  GO:0030337 DNA polymerase processivity factor activ...         1           1     0.01               4  0.0084 1.000 0.0084 0.0084
5  GO:0047077 Photinus-luciferin 4-monooxygenase (ATP-...         1           1     0.01               5  0.0084 1.000 0.0084 0.0084
6  GO:0004421 hydroxymethylglutaryl-CoA synthase activ...         2           1     0.02               8  0.0167 0.962 0.0167 0.0167
7  GO:0008703 5-amino-6-(5-phosphoribosylamino)uracil ...         2           1     0.02               9  0.0167 0.996 0.0167 0.0167
8  GO:0046873              metal ion transporter activity        34           2     0.28              12  0.0324 0.635 0.0324 0.2192
9  GO:0003906 DNA-(apurinic or apyrimidinic site) lyas...         4           1     0.03              13  0.0330 0.714 0.0330 0.0330
10 GO:0003950        NAD+ ADP-ribosyltransferase activity         4           1     0.03              14  0.0330 0.086 0.0330 0.0330
11 GO:0004186                carboxypeptidase C activity         4           1     0.03              15  0.0330 0.320 0.0330 0.0330
12 GO:0005385               zinc ion transporter activity         4           1     0.03              16  0.0330 0.846 0.0330 0.0330

> ##########  Cellular component  #############

None

> ##########  Biological process  #############

    GO.ID                                    Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1  GO:0006303 double-strand break repair via nonhomolo...         2           2     0.02               1 6.9e-05 1.00 6.9e-05 6.9e-05
2  GO:0006275               regulation of DNA replication         1           1     0.01              10 0.00841 1.00  0.0084  0.0084
3  GO:0006471         protein amino acid ADP-ribosylation         1           1     0.01              11 0.00841 1.00  0.0084  0.0084
4  GO:0050896                      response to stimulus       182           7     1.53               7 0.00068 0.29  0.0133  1.0000
5  GO:0006281                                DNA repair        74           5     0.62               4 0.00034 0.53  0.0191  0.0191
6  GO:0006974            response to DNA damage stimulus        74           5     0.62               5 0.00034 0.53  0.0191  1.0000
7  GO:0009719            response to endogenous stimulus        74           5     0.62               6 0.00034 0.53  0.0191  1.0000
8  GO:0006829                        zinc ion transport         4           1     0.03              13 0.03322 0.84  0.0332  0.0332
9  GO:0006950                        response to stress       100           5     0.84               8 0.00136 0.74  0.0424  1.0000

##############################################
##                                          ##
##              Group C                     ##
##                                          ##
##############################################

> ##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS    elim  weight
```

1	GO:0003995	acyl-CoA dehydrogenase activity	10	4	0.19	1	2.5e-05	0.9999	2.5e-05	2.5e-05
2	GO:0004252	serine-type endopeptidase activity	39	5	0.75	2	0.00082	0.3926	0.00082	0.00082
3	GO:0003700	transcription factor activity	324	15	6.23	4	0.00122	0.1490	0.00122	0.00122
4	GO:0008270	zinc ion binding	649	22	12.47	10	0.00523	0.0047	0.00523	0.41024
5	GO:0051213	dioxygenase activity	20	3	0.38	11	0.00620	0.7333	0.00620	1.00000
6	GO:0004467	long-chain-fatty-acid-CoA ligase activit...	7	2	0.13	13	0.00721	0.9995	0.00721	0.00721
7	GO:0004871	signal transducer activity	91	6	1.75	14	0.00779	0.0166	0.00779	0.16447
8	GO:0030234	enzyme regulator activity	95	6	1.83	16	0.00955	0.2710	0.00955	1.00000
9	GO:0000907	sulfonate dioxygenase activity	1	1	0.02	19	0.01922	0.9996	0.01922	0.01922
10	GO:0003952	NAD+ synthase (glutamine-hydrolyzing) ac...	1	1	0.02	20	0.01922	0.9997	0.01922	0.01922
11	GO:0004028	3-chloroallyl aldehyde dehydrogenase act...	1	1	0.02	21	0.01922	0.9998	0.01922	0.01922
12	GO:0004133	glycogen debranching enzyme activity	1	1	0.02	22	0.01922	0.9995	0.01922	1.00000
13	GO:0004134	4-alpha-glucanotransferase activity	1	1	0.02	23	0.01922	0.9995	0.01922	0.01922
14	GO:0004135	amylo-alpha-1,6-glucosidase activity	1	1	0.02	24	0.01922	0.9995	0.01922	0.01922
15	GO:0004361	glutaryl-CoA dehydrogenase activity	1	1	0.02	25	0.01922	0.9995	0.01922	1.00000
16	GO:0004368	glycerol-3-phosphate dehydrogenase activ...	1	1	0.02	26	0.01922	0.9997	0.01922	0.01922
17	GO:0004370	glycerol kinase activity	1	1	0.02	27	0.01922	0.9994	0.01922	0.01922
18	GO:0004529	exodeoxyribonuclease activity	1	1	0.02	28	0.01922	0.9994	0.01922	1.00000
19	GO:0004746	riboflavin synthase activity	1	1	0.02	29	0.01922	0.9995	0.01922	0.01922
20	GO:0005498	sterol carrier activity	1	1	0.02	30	0.01922	1.0000	0.01922	0.01922
21	GO:0008852	exodeoxyribonuclease I activity	1	1	0.02	31	0.01922	0.9994	0.01922	0.01922
22	GO:0016895	exodeoxyribonuclease activity, producing...	1	1	0.02	32	0.01922	0.9994	0.01922	1.00000
23	GO:0016995	cholesterol oxidase activity	1	1	0.02	33	0.01922	0.9993	0.01922	0.01922
24	GO:0018580	2-nitropropane dioxygenase activity	1	1	0.02	34	0.01922	0.9999	0.01922	0.01922
25	GO:0018602	2,4-dichlorophenoxyacetate alpha-ketoglu...	1	1	0.02	35	0.01922	0.9996	0.01922	0.01922
26	GO:0019798	procollagen-proline dioxygenase activity	1	1	0.02	36	0.01922	0.9996	0.01922	0.01922
27	GO:0031543	peptidyl-proline dioxygenase activity	1	1	0.02	37	0.01922	0.9996	0.01922	1.00000
28	GO:0045432	leucoanthocyanidin dioxygenase activity	1	1	0.02	38	0.01922	0.9996	0.01922	0.01922
29	GO:0045442	deacetoxycephalosporin C hydroxylase act...	1	1	0.02	39	0.01922	0.9996	0.01922	0.01922
30	GO:0016796	exonuclease activity, active with either...	12	2	0.23	40	0.02130	0.0872	0.02130	1.00000
31	GO:0019207	kinase regulator activity	58	4	1.11	41	0.02473	0.1333	0.02473	1.00000
32	GO:0019887	protein kinase regulator activity	58	4	1.11	42	0.02473	0.1333	0.02473	1.00000
33	GO:0008603	cAMP-dependent protein kinase regulator ...	35	3	0.67	43	0.02893	0.3339	0.02893	0.02893
34	GO:0003684	damaged DNA binding	16	2	0.31	44	0.03684	0.5079	0.03684	0.03684
35	GO:0008081	phosphoric diester hydrolase activity	16	2	0.31	45	0.03684	0.9300	0.03684	0.03684
36	GO:0016702	oxidoreductase activity, acting on singl...	16	2	0.31	46	0.03684	0.9434	0.03684	1.00000
37	GO:0003697	single-stranded DNA binding	2	1	0.04	47	0.03807	0.9989	0.03807	0.03807
38	GO:0004658	propionyl-CoA carboxylase activity	2	1	0.04	48	0.03807	0.9998	0.03807	0.03807
39	GO:0005496	steroid binding	2	1	0.04	49	0.03807	0.9999	0.03807	1.00000
40	GO:0008470	isovaleryl-CoA dehydrogenase activity	2	1	0.04	50	0.03807	0.9994	0.03807	1.00000
41	GO:0008889	glycerophosphodiester phosphodiesterase ...	2	1	0.04	51	0.03807	0.5299	0.03807	1.00000
42	GO:0043566	structure-specific DNA binding	2	1	0.04	52	0.03807	0.9989	0.03807	1.00000
43	GO:0016701	oxidoreductase activity, acting on singl...	17	2	0.33	53	0.04124	0.7950	0.04124	1.00000

```
> ##########  Cellular component  #############
```

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0005634	nucleus	695	23	13.78	1	0.0031	2.5e-05	0.0031	0.0031
2	GO:0009349	riboflavin synthase complex	1	1	0.02	2	0.0198	0.99941	0.0198	0.0198
3	GO:0019008	molybdopterin synthase complex	1	1	0.02	3	0.0198	0.99993	0.0198	0.0198
4	GO:0005952	cAMP-dependent protein kinase complex	35	3	0.69	6	0.0307	0.16380	0.0307	0.0307

```
> ##########  Biological process  #############
```

```
       GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS   elim  weight
1  GO:0006072      glycerol-3-phosphate metabolic process         4           2     0.07               4 0.00181 1.00 0.0018 1.00000
2  GO:0006355 regulation of transcription, DNA-depende...       395          15     6.98               5 0.00338 0.17 0.0034 0.00338
3  GO:0005977                   glycogen metabolic process         2           1     0.04              18 0.03505 1.00 0.0351 1.00000
4  GO:0005978               glycogen biosynthetic process         2           1     0.04              19 0.03505 1.00 0.0351 0.03505
5  GO:0007154                         cell communication       144           6     2.55              20 0.04098 0.72 0.0410 1.00000
6  GO:0007165                        signal transduction       144           6     2.55              21 0.04098 0.72 0.0410 0.33095
7  GO:0043283               biopolymer metabolic process      1100          32    19.45               3 0.00131 0.15 0.0431 0.90305
8  GO:0006508                                 proteolysis       271           9     4.79              23 0.04828 0.15 0.0483 0.11595

############################################
##                                        ##
##               Group E                  ##
##                                        ##
############################################

> ##########  Metabolic function  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS   elim weight
1  GO:0000293          ferric-chelate reductase activity         8           2     0.06               1  0.0017 0.339 0.0017 0.0017
2  GO:0009899              ent-kaurene synthase activity         1           1     0.01               4  0.0080 1.000 0.0080 0.0080
3  GO:0016888 endodeoxyribonuclease activity, producin...         2           1     0.02               5  0.0160 0.728 0.0160 0.0160
4  GO:0004190        aspartic-type endopeptidase activity        25           2     0.20               6  0.0167 0.961 0.0167 0.0167
5  GO:0000721     (R,R)-butanediol dehydrogenase activity         3           1     0.02               7  0.0238 0.622 0.0238 0.0238
6  GO:0003978            UDP-glucose 4-epimerase activity         3           1     0.02               8  0.0238 0.712 0.0238 0.0238
7  GO:0004520             endodeoxyribonuclease activity         3           1     0.02               9  0.0238 0.923 0.0238 1.0000
8  GO:0004553 hydrolase activity, hydrolyzing O-glycos...       223           5     1.79              10  0.0316 0.097 0.0316 0.3978
9  GO:0004536                  deoxyribonuclease activity         4           1     0.03              11  0.0317 0.529 0.0317 1.0000
10 GO:0004557               alpha-galactosidase activity         4           1     0.03              12  0.0317 0.231 0.0317 0.0317
11 GO:0005275                 amine transporter activity        87           3     0.70              13  0.0319 0.999 0.0319 1.0000
12 GO:0005279 amino acid-polyamine transporter activit...        87           3     0.70              14  0.0319 0.999 0.0319 0.0319
13 GO:0015171             amino acid transporter activity        87           3     0.70              15  0.0319 0.999 0.0319 1.0000
14 GO:0015203              polyamine transporter activity        87           3     0.70              16  0.0319 0.999 0.0319 1.0000
15 GO:0016798 hydrolase activity, acting on glycosyl b...       225           5     1.80              17  0.0327 0.096 0.0327 0.5124
16 GO:0005342           organic acid transporter activity        89           3     0.71              18  0.0338 0.993 0.0338 1.0000
17 GO:0046943        carboxylic acid transporter activity        89           3     0.71              19  0.0338 0.993 0.0338 1.0000
18 GO:0015290 electrochemical potential-driven transpo...       235           5     1.88              20  0.0384 0.818 0.0384 1.0000
19 GO:0015291                              porter activity       235           5     1.88              21  0.0384 0.818 0.0384 0.4868
20 GO:0005375            copper ion transporter activity         5           1     0.04              22  0.0394 0.733 0.0394 0.0394
21 GO:0008807 carboxyvinyl-carboxyphosphonate phosphor...         5           1     0.04              23  0.0394 0.798 0.0394 0.0394
22 GO:0016769 transferase activity, transferring nitro...        41           2     0.33              25  0.0422 0.848 0.0422 0.0422

> ##########  Cellular component  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0016020                                 membrane      1079          12     6.51               1   0.003  0.3863 0.003  0.014

> ##########  Biological process  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS  elim weight
1  GO:0005975             carbohydrate metabolic process       302           6     2.34               1   0.027 0.8693 0.027  0.047
2  GO:0006865                       amino acid transport        87           3     0.68               2   0.029 0.9582 0.029  0.029
```

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3  GO:0015837                           amine transport        87           3     0.68               3   0.029 0.9582 0.029  1.000
4  GO:0015849                     organic acid transport        87           3     0.68               4   0.029 0.9582 0.029  1.000
5  GO:0046942                  carboxylic acid transport        87           3     0.68               5   0.029 0.9582 0.029  1.000
6  GO:0009225         nucleotide-sugar metabolic process         4           1     0.03               6   0.031 0.3932 0.031  0.031
7  GO:0006825                       copper ion transport         6           1     0.05               7   0.046 0.5440 0.046  0.046

##############################################
##                                          ##
##              Group F                    ##
##                                          ##
##############################################

> ##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS   elim  weight
1  GO:0015075                ion transporter activity       206          20     8.72               3 0.00040 0.98 0.0004 1.00000
2  GO:0008236            serine-type peptidase activity        60          11     2.54               1 3.4e-05 0.76 0.0014 0.00047
3  GO:0004004     ATP-dependent RNA helicase activity        42           7     1.78               4 0.00169 0.28 0.0017 0.00169
4  GO:0015462    protein-transporting ATPase activity        42           7     1.78               5 0.00169 0.28 0.0017 0.00169
5  GO:0015616                DNA translocase activity        42           7     1.78               6 0.00169 0.28 0.0017 0.00169
6  GO:0017116 single-stranded DNA-dependent ATP-depend...        42           7     1.78               7 0.00169 0.28 0.0017 0.00169
7  GO:0042624                ATPase activity, uncoupled        42           7     1.78               8 0.00169 0.28 0.0017 0.00169
8  GO:0003993                 acid phosphatase activity        15           4     0.64              13 0.00296 0.68 0.0030 0.00296
9  GO:0003725               double-stranded RNA binding         3           2     0.13              17 0.00521 0.66 0.0052 0.00521
10 GO:0004252          serine-type endopeptidase activity        39           6     1.65              19 0.00546 0.55 0.0055 1.00000
11 GO:0004364            glutathione transferase activity        10           3     0.42              22 0.00721 0.26 0.0072 0.00721
12 GO:0005355                glucose transporter activity         4           2     0.17              23 0.01013 1.00 0.0101 0.01013
13 GO:0005385               zinc ion transporter activity         4           2     0.17              24 0.01013 0.51 0.0101 0.01013
14 GO:0008240             tripeptidyl-peptidase activity         4           2     0.17              25 0.01013 0.56 0.0101 1.00000
15 GO:0015145         monosaccharide transporter activity         4           2     0.17              26 0.01013 1.00 0.0101 1.00000
16 GO:0015149                hexose transporter activity         4           2     0.17              27 0.01013 1.00 0.0101 1.00000
17 GO:0019131           tripeptidyl-peptidase I activity         4           2     0.17              28 0.01013 0.56 0.0101 0.01013
18 GO:0005215                       transporter activity       843          57    35.70               2 0.00014 0.99 0.0127 0.06404
19 GO:0046873             metal ion transporter activity        34           5     1.44              31 0.01330 0.70 0.0133 0.12980
20 GO:0050236         pyridoxine 4-dehydrogenase activity         5           2     0.21              32 0.01641 0.71 0.0164 0.01641
21 GO:0004185            serine carboxypeptidase activity        14           3     0.59              33 0.01930 0.93 0.0193 1.00000
22 GO:0042625 ATPase activity, coupled to transmembran...        97           9     4.11              34 0.02100 0.70 0.0210 0.02100
23 GO:0004289                        subtilase activity        18           3     0.76              40 0.03823 0.12 0.0382 1.00000
24 GO:0003883                    CTP synthase activity         1           1     0.04              41 0.04235 1.00 0.0423 0.04235
25 GO:0003963           RNA-3'-phosphate cyclase activity         1           1     0.04              42 0.04235 1.00 0.0423 0.04235
26 GO:0004045           aminoacyl-tRNA hydrolase activity         1           1     0.04              43 0.04235 1.00 0.0423 0.04235
27 GO:0004145        diamine N-acetyltransferase activity         1           1     0.04              44 0.04235 1.00 0.0423 0.04235
28 GO:0004360 glutamine-fructose-6-phosphate transamin...         1           1     0.04              45 0.04235 1.00 0.0423 0.04235
29 GO:0004750     ribulose-phosphate 3-epimerase activity         1           1     0.04              46 0.04235 1.00 0.0423 0.04235
30 GO:0004851 uroporphyrin-III C-methyltransferase act...         1           1     0.04              47 0.04235 1.00 0.0423 0.04235
31 GO:0017096 acetylserotonin O-methyltransferase acti...         1           1     0.04              48 0.04235 1.00 0.0423 0.04235
32 GO:0015036           disulfide oxidoreductase activity        46           5     1.95              49 0.04360 1.00 0.0436 0.04360
33 GO:0003899        DNA-directed RNA polymerase activity        33           4     1.40              51 0.04901 0.82 0.0490 0.04901

> ##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS    elim weight
1  GO:0016020                                membrane      1079          63    44.18               1 5.7e-05 0.943 5.7e-05 0.0032
```

```
2  GO:0031966                      mitochondrial membrane        40           5     1.64               2   0.022 0.836   0.022 1.0000
3  GO:0016021                        integral to membrane       698          38    28.58               3   0.023 0.035   0.023 0.0267
4  GO:0031224                       intrinsic to membrane       698          38    28.58               4   0.023 0.035   0.023 0.2741
5  GO:0044425                              membrane part       734          39    30.06               5   0.030 0.074   0.030 1.0000
6  GO:0031967                         organelle envelope        62           6     2.54               6   0.039 0.779   0.039 1.0000
7  GO:0005740                      mitochondrial envelope        47           5     1.92               7   0.041 0.794   0.041 1.0000
8  GO:0005742 mitochondrial outer membrane translocase...         1           1     0.04               8   0.041 0.998   0.041 0.0409
9  GO:0009316       3-isopropylmalate dehydratase complex         1           1     0.04               9   0.041 1.000   0.041 0.0409

> ##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS   elim weight
1  GO:0006810                                transport       940          58    38.91               1 0.00055 0.995 0.0012 0.3841
2  GO:0006829                          zinc ion transport         4           2     0.17               4 0.00968 0.490 0.0097 0.0097
3  GO:0015074                             DNA integration         1           1     0.04               8 0.04140 0.997 0.0414 0.0414

##############################################
##                                          ##
##                Group G                   ##
##                                          ##
##############################################

> ##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS    elim  weight
1  GO:0004364            glutathione transferase activity        10           2     0.04               1 0.00084 0.2763 0.00084 0.00084
2  GO:0004344 glucose dehydrogenase (acceptor) activit...        12           2     0.05               2 0.00122 0.7808 0.00122 0.00122

> ##########  Cellular component  #############

    GO.ID                                 Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0009986                         cell surface         1           1     0.00               1  0.0039  1.0000 0.0039 0.0039

>
> ##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS  elim weight
1  GO:0006526               arginine biosynthetic process         8           1     0.03               1   0.027 0.82 0.027  0.027
2  GO:0016998                 cell wall catabolic process        10           1     0.03               2   0.034 0.35 0.034  0.034
3  GO:0006865                        amino acid transport        87           2     0.30               3   0.035 0.86 0.035  0.035
4  GO:0015837                             amine transport        87           2     0.30               4   0.035 0.86 0.035  1.000
5  GO:0015849                      organic acid transport        87           2     0.30               5   0.035 0.86 0.035  1.000
6  GO:0046942                   carboxylic acid transport        87           2     0.30               6   0.035 0.86 0.035  1.000

##############################################
##                                          ##
##                Group H                   ##
##                                          ##
##############################################

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS   elim weight
1  GO:0003852        2-isopropylmalate synthase activity         1           1     0.00               2  0.0043 1.0000 0.0043 1.0000
2  GO:0004470                      malic enzyme activity         2           1     0.01               3  0.0085 1.0000 0.0085 0.0085
```

```
3  GO:0017076                   purine nucleotide binding       759           8     3.24               4  0.0107 0.7929 0.0107 0.0178
4  GO:0003978            UDP-glucose 4-epimerase activity         3           1     0.01               5  0.0128 0.9999 0.0128 0.0128
5  GO:0004086       carbamoyl-phosphate synthase activity         3           1     0.01               6  0.0128 0.6711 0.0128 0.0128
6  GO:0047681 aryl-alcohol dehydrogenase (NADP+) activ...         3           1     0.01               7  0.0128 0.3568 0.0128 0.0128
7  GO:0000166                          nucleotide binding       785           8     3.35               8  0.0130 0.6489 0.0130 0.3870
8  GO:0030554                  adenyl nucleotide binding       668           7     2.85               9  0.0183 0.9031 0.0183 0.3710
9  GO:0004197        cysteine-type endopeptidase activity        57           2     0.24              11  0.0242 0.7754 0.0242 0.0242
10 GO:0016630      protochlorophyllide reductase activity         6           1     0.03              12  0.0254 0.3579 0.0254 0.0254
11 GO:0016857 racemase and epimerase activity, acting ...         8           1     0.03              13  0.0337 0.9257 0.0337 1.0000
12 GO:0008234            cysteine-type peptidase activity        69           2     0.29              14  0.0345 0.5519 0.0345 1.0000
13 GO:0008812              choline dehydrogenase activity         9           1     0.04              15  0.0378 0.0424 0.0378 0.0378
14 GO:0003723                                RNA binding        76           2     0.32              16  0.0411 0.6485 0.0411 0.0411
15 GO:0005524                                ATP binding       627           6     2.68              17  0.0439 0.9393 0.0439 1.0000
16 GO:0046912 transferase activity, transferring acyl ...        13           2     0.06               1  0.0013 0.6972 0.0481 0.0013


> ##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0030688 nucleolar preribosome, small subunit pre...         1           1     0.00               1  0.0022 1.00000 0.0022 0.0022

> ##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS   elim weight
1  GO:0006405                    RNA export from nucleus         1           1     0.00               1  0.0045 1.000 0.0045 0.0045
2  GO:0008612 hypusine biosynthetic process from pepti...         1           1     0.00               2  0.0045 1.000 0.0045 0.0045
3  GO:0050983 spermidine catabolic process to deoxyhyp...         1           1     0.00               3  0.0045 1.000 0.0045 0.0045
4  GO:0044262     cellular carbohydrate metabolic process       106           3     0.48              11  0.0114 0.873 0.0114 1.0000
5  GO:0006551                   leucine metabolic process         4           1     0.02              19  0.0180 1.000 0.0180 1.0000
6  GO:0009098                leucine biosynthetic process         4           1     0.02              20  0.0180 1.000 0.0180 0.0180
7  GO:0009225          nucleotide-sugar metabolic process         4           1     0.02              21  0.0180 0.937 0.0180 0.0180
8  GO:0006108                   malate metabolic process         5           1     0.02              23  0.0224 0.953 0.0224 0.0224
9  GO:0006364                             rRNA processing         5           1     0.02              24  0.0224 0.888 0.0224 0.0224
10 GO:0016072                    rRNA metabolic process         5           1     0.02              25  0.0224 0.888 0.0224 1.0000
11 GO:0006092 main pathways of carbohydrate metabolic ...        59           2     0.27              26  0.0286 0.970 0.0286 0.2094
12 GO:0006100 tricarboxylic acid cycle intermediate me...         7           1     0.03              27  0.0313 0.979 0.0313 1.0000
13 GO:0043648         dicarboxylic acid metabolic process         7           1     0.03              28  0.0313 0.701 0.0313 1.0000
14 GO:0015980 energy derivation by oxidation of organi...        68           2     0.31              30  0.0372 0.969 0.0372 1.0000
15 GO:0006012                 galactose metabolic process         9           1     0.04              31  0.0401 0.978 0.0401 0.0401
16 GO:0006396                           RNA processing        76           2     0.34              32  0.0455 0.040 0.0455 0.2662
17 GO:0042254            ribosome biogenesis and assembly        11           1     0.05              33  0.0487 0.995 0.0487 1.0000

##############################################
##                                          ##
##              Group I                     ##
##                                          ##
##############################################

> ##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS    elim  weight
1  GO:0005351                    sugar porter activity        99          17     4.44               1 1.4e-06  0.9993 1.4e-06 1.4e-06
2  GO:0016207            4-coumarate-CoA ligase activity        11           4     0.49               9 0.00101  0.3585  0.0010 1.00000
```

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3  GO:0008410                    CoA-transferase activity         3           2     0.13              13 0.00583  0.9980  0.0058 0.00583
4  GO:0016421                    CoA carboxylase activity         3           2     0.13              14 0.00583  0.9987  0.0058 1.00000
5  GO:0016491                     oxidoreductase activity      1146          68    51.39              15 0.00607  0.0184  0.0061 0.29894
6  GO:0004553 hydrolase activity, hydrolyzing O-glycos...       223          18    10.00              17 0.01074  0.1136  0.0107 0.15701
7  GO:0008733              L-arabinose isomerase activity        55           7     2.47              18 0.01079  0.4786  0.0108 0.01079
8  GO:0016798 hydrolase activity, acting on glycosyl b...       225          18    10.09              19 0.01171  0.1115  0.0117 0.34402
9  GO:0046914                transition metal ion binding       752          46    33.72              20 0.01543  0.0141  0.0154 0.01543
10 GO:0043169                             cation binding       812          49    36.41              21 0.01578  0.0231  0.0158 0.24416
11 GO:0003988       acetyl-CoA C-acyltransferase activity         5           2     0.22              22 0.01831  0.6018  0.0183 0.01831
12 GO:0046556        alpha-N-arabinofuranosidase activity         5           2     0.22              23 0.01831  0.8177  0.0183 0.01831
13 GO:0043167                               ion binding       840          50    37.67              24 0.01876  0.0175  0.0188 1.00000
14 GO:0046872                           metal ion binding       840          50    37.67              25 0.01876  0.0175  0.0188 0.27921
15 GO:0016620 oxidoreductase activity, acting on the a...        35           5     1.57              26 0.01879  0.8950  0.0188 0.01879
16 GO:0016616 oxidoreductase activity, acting on the C...       188          15     8.43              27 0.02096  0.0030  0.0210 0.58353
17 GO:0003825 alpha,alpha-trehalose-phosphate synthase...         6           2     0.27              28 0.02665  0.9585  0.0267 0.02665
18 GO:0004396                        hexokinase activity         6           2     0.27              29 0.02665  0.9992  0.0267 0.02665
19 GO:0050112          inositol 2-dehydrogenase activity         6           2     0.27              30 0.02665  0.1459  0.0267 0.02665
20 GO:0016861 intramolecular oxidoreductase activity, ...        67           7     3.00              31 0.02944  0.7641  0.0294 1.00000
21 GO:0016746 transferase activity, transferring acyl ...       130          11     5.83              32 0.03083  0.7225  0.0308 0.85161
22 GO:0016903 oxidoreductase activity, acting on the a...        41           5     1.84              33 0.03495  0.9048  0.0349 1.00000
23 GO:0004029       aldehyde dehydrogenase (NAD) activity         7           2     0.31              34 0.03622  0.7397  0.0362 1.00000
24 GO:0003824                        catalytic activity      3853         194   172.77              10 0.00161 2.4e-07  0.0371 0.75565
25 GO:0016885 ligase activity, forming carbon-carbon b...         4           3     0.18               6 0.00034  1.0000  0.0445 0.00034
26 GO:0003996                    acyl-CoA ligase activity         1           1     0.04              35 0.04484  0.9962  0.0448 1.00000
27 GO:0004059 aralkylamine N-acetyltransferase activit...         1           1     0.04              36 0.04484  0.9994  0.0448 0.04484
28 GO:0004076                    biotin synthase activity         1           1     0.04              37 0.04484  0.9979  0.0448 0.04484
29 GO:0004474                    malate synthase activity         1           1     0.04              38 0.04484  0.9975  0.0448 0.04484
30 GO:0004485    methylcrotonoyl-CoA carboxylase activity         1           1     0.04              39 0.04484  0.9964  0.0448 1.00000
31 GO:0004559                  alpha-mannosidase activity         1           1     0.04              40 0.04484  0.9980  0.0448 0.04484
32 GO:0004736                pyruvate carboxylase activity         1           1     0.04              41 0.04484  1.0000  0.0448 1.00000
33 GO:0008108 UDP-glucose:hexose-1-phosphate uridylylt...         1           1     0.04              42 0.04484  0.9994  0.0448 0.04484
34 GO:0008824                    cyanate hydratase activity         1           1     0.04              43 0.04484  1.0000  0.0448 0.04484
35 GO:0009013 succinate-semialdehyde dehydrogenase [NA...         1           1     0.04              44 0.04484  0.9977  0.0448 1.00000
36 GO:0018853            perillyl-CoA synthetase activity         1           1     0.04              45 0.04484  0.9962  0.0448 1.00000
37 GO:0018854 3-isopropenyl-6-oxoheptanoyl-CoA synthet...         1           1     0.04              46 0.04484  0.9962  0.0448 1.00000
38 GO:0018855 2-oxo-delta3-4,5,5-trimethylcyclopenteny...         1           1     0.04              47 0.04484  0.9962  0.0448 1.00000
39 GO:0018856          benzoyl acetate-CoA ligase activity         1           1     0.04              48 0.04484  0.9962  0.0448 1.00000
40 GO:0018857    2,4-dichlorobenzoate-CoA ligase activity         1           1     0.04              49 0.04484  0.9962  0.0448 1.00000
41 GO:0000293           ferric-chelate reductase activity         8           2     0.36              50 0.04689  0.7904  0.0469 0.04689
42 GO:0008270                             zinc ion binding       649          38    29.10              51 0.04886  0.0267  0.0489 0.57157

> ##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0016021                    integral to membrane       698          38    26.18               1  0.0043 0.02509 0.0043 0.0043
2  GO:0019012                                 virion         1           1     0.04               5  0.0375 0.99866 0.0375 1.0000
3  GO:0019028                           viral capsid         1           1     0.04               6  0.0375 0.99866 0.0375 0.0375
4  GO:0044423                            virion part         1           1     0.04               7  0.0375 0.99866 0.0375 1.0000

> ##########  Biological process  #############

    GO.ID                                  Term Annotated Significant Expected Rank in classic classic     KS    elim  weight
1  GO:0008643                carbohydrate transport       101          17     4.66               1 2.6e-06 0.9981 2.6e-06 2.6e-06
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2  GO:0005975              carbohydrate metabolic process       302          30    13.93              2 4.1e-05 0.9981  0.0032  0.0051
3  GO:0006097                           glyoxylate cycle         3           2     0.14              4  0.0062 0.7649  0.0062  0.0062
4  GO:0005996           monosaccharide metabolic process        51           7     2.35              7  0.0083 0.9994  0.0083  1.0000
5  GO:0006091 generation of precursor metabolites and ...       693          45    31.98              8  0.0089 0.0546  0.0181  0.3376
6  GO:0019566                arabinose metabolic process         5           2     0.23              9  0.0193 0.8117  0.0193  1.0000
7  GO:0046373              L-arabinose metabolic process         5           2     0.23             10  0.0193 0.8117  0.0193  0.0193
8  GO:0016051          carbohydrate biosynthetic process        24           4     1.11             11  0.0226 0.8122  0.0226  1.0000
9  GO:0005992             trehalose biosynthetic process         6           2     0.28             12  0.0281 0.9268  0.0281  0.0281
10 GO:0046351          disaccharide biosynthetic process         6           2     0.28             13  0.0281 0.9268  0.0281  1.0000
11 GO:0006118                        electron transport       599          37    27.64             15  0.0358 0.0047  0.0358  0.0358
12 GO:0005984           disaccharide metabolic process         7           2     0.32             17  0.0382 0.7264  0.0382  1.0000
13 GO:0005991              trehalose metabolic process         7           2     0.32             18  0.0382 0.7264  0.0382  1.0000
14 GO:0019321                pentose metabolic process         7           2     0.32             19  0.0382 0.6153  0.0382  1.0000
15 GO:0006768                 biotin metabolic process         1           1     0.05             20  0.0461 0.9979  0.0461  1.0000
16 GO:0009102              biotin biosynthetic process         1           1     0.05             21  0.0461 0.9979  0.0461  0.0461
17 GO:0009439                cyanate metabolic process         1           1     0.05             22  0.0461 1.0000  0.0461  0.0461
18 GO:0009069 serine family amino acid metabolic proce...       30           4     1.38             23  0.0472 0.9191  0.0472  1.0000
19 GO:0006564              L-serine biosynthetic process        18           3     0.83             24  0.0474 0.5620  0.0474  0.0474

##############################################
##                                          ##
##              Group J                     ##
##                                          ##
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##########  Metabolic function  #############

     GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS    elim  weight
1   GO:0005524                              ATP binding       627         227   158.65              6 7.8e-11 0.998 7.8e-11 7.8e-11
2   GO:0004713           protein-tyrosine kinase activity       119          61    30.11             10 7.6e-10 0.993 7.6e-10 2.8e-08
3   GO:0005515                           protein binding       125          67    31.63              5 7.8e-12 0.928 3.9e-09 1.8e-11
4   GO:0005525                              GTP binding        94          46    23.78             19 5.5e-07 0.966 5.5e-07 5.5e-07
5   GO:0004298           threonine endopeptidase activity        16          13     4.05             28 4.2e-06 0.976 4.2e-06 4.2e-06
6   GO:0004842          ubiquitin-protein ligase activity        77          37    19.48             29 1.2e-05 0.970 1.2e-05 1.2e-05
7   GO:0004376    glycolipid mannosyltransferase activity        10           9     2.53             33 3.2e-05 0.996 3.2e-05 1.00000
8   GO:0008605      protein kinase CK2 regulator activity        34          20     8.60             34 3.3e-05 0.932 3.3e-05 3.3e-05
9   GO:0003676                       nucleic acid binding      1047         338   264.92             14 1.0e-08 0.622 3.5e-05 1.0e-06
10  GO:0004576        oligosaccharyl transferase activity        12          10     3.04             37 4.1e-05 0.909 4.1e-05 4.1e-05
11  GO:0004682                protein kinase CK2 activity        33          19     8.35             40 7.8e-05 0.779 7.8e-05 1.00000
12  GO:0004691     cAMP-dependent protein kinase activity        33          19     8.35             41 7.8e-05 0.779 7.8e-05 1.00000
13  GO:0004674   protein serine/threonine kinase activity       153          73    38.71             11 1.1e-09 0.999 0.00013 4.5e-08
14  GO:0008603 cAMP-dependent protein kinase regulator ...        35          19     8.86             44 0.00023 0.767 0.00023 0.00023
15  GO:0005509                         calcium ion binding        63          29    15.94             46 0.00027 0.962 0.00027 0.00027
16  GO:0003684                         damaged DNA binding        16          11     4.05             47 0.00031 0.954 0.00031 0.00031
17  GO:0003889              alpha DNA polymerase activity        17          11     4.30             57 0.00069 0.861 0.00069 1.00000
18  GO:0003891              delta DNA polymerase activity        17          11     4.30             58 0.00069 0.861 0.00069 1.00000
19  GO:0003893            epsilon DNA polymerase activity        17          11     4.30             59 0.00069 0.861 0.00069 1.00000
20  GO:0003894               zeta DNA polymerase activity        17          11     4.30             60 0.00069 0.861 0.00069 1.00000
21  GO:0003895 gamma DNA-directed DNA polymerase activi...        17          11     4.30             61 0.00069 0.861 0.00069 1.00000
22  GO:0015999                eta DNA polymerase activity        17          11     4.30             62 0.00069 0.861 0.00069 1.00000
23  GO:0016000               iota DNA polymerase activity        17          11     4.30             63 0.00069 0.861 0.00069 1.00000
24  GO:0016448                 mu DNA polymerase activity        17          11     4.30             64 0.00069 0.861 0.00069 1.00000
25  GO:0016449             lambda DNA polymerase activity        17          11     4.30             65 0.00069 0.861 0.00069 1.00000
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26	GO:0016450	kappa DNA polymerase activity	17	11	4.30	66	0.00069	0.861	0.00069	1.00000
27	GO:0016451	nu DNA polymerase activity	17	11	4.30	67	0.00069	0.861	0.00069	1.00000
28	GO:0016452	theta DNA polymerase activity	17	11	4.30	68	0.00069	0.861	0.00069	1.00000
29	GO:0019984	sigma DNA polymerase activity	17	11	4.30	69	0.00069	0.861	0.00069	1.00000
30	GO:0008235	metalloexopeptidase activity	30	16	7.59	70	0.00091	0.862	0.00091	0.00101
31	GO:0008026	ATP-dependent helicase activity	89	36	22.52	71	0.00113	0.804	0.00113	0.00113
32	GO:0003890	beta DNA polymerase activity	18	11	4.55	74	0.00136	0.854	0.00136	1.00000
33	GO:0000009	alpha-1,6-mannosyltransferase activity	7	6	1.77	75	0.00143	0.872	0.00143	1.00000
34	GO:0000026	alpha-1,2-mannosyltransferase activity	7	6	1.77	76	0.00143	0.872	0.00143	1.00000
35	GO:0000033	alpha-1,3-mannosyltransferase activity	7	6	1.77	77	0.00143	0.872	0.00143	1.00000
36	GO:0003682	chromatin binding	7	6	1.77	78	0.00143	0.827	0.00143	0.00143
37	GO:0003980	UDP-glucose:glycoprotein glucosyltransfe...	7	6	1.77	79	0.00143	0.872	0.00143	0.00143
38	GO:0004583	dolichyl-phosphate-glucose-glycolipid al...	7	6	1.77	80	0.00143	0.872	0.00143	0.00143
39	GO:0008376	acetylgalactosaminyltransferase activity	7	6	1.77	81	0.00143	0.872	0.00143	0.00143
40	GO:0008921	lipopolysaccharide-1,6-galactosyltransfe...	7	6	1.77	82	0.00143	0.872	0.00143	1.00000
41	GO:0016253	UDP-N-acetylglucosamine-peptide N-acetyl...	7	6	1.77	83	0.00143	0.872	0.00143	0.00143
42	GO:0016759	cellulose synthase activity	7	6	1.77	84	0.00143	0.872	0.00143	0.00143
43	GO:0018715	9-phenanthrol UDP-glucuronosyltransferas...	7	6	1.77	85	0.00143	0.872	0.00143	0.00143
44	GO:0018716	1-phenanthrol glycosyltransferase activi...	7	6	1.77	86	0.00143	0.872	0.00143	0.00143
45	GO:0018717	9-phenanthrol glycosyltransferase activi...	7	6	1.77	87	0.00143	0.872	0.00143	0.00143
46	GO:0018718	1,2-dihydroxy-phenanthrene glycosyltrans...	7	6	1.77	88	0.00143	0.872	0.00143	0.00143
47	GO:0019187	beta-1,4-mannosyltransferase activity	7	6	1.77	89	0.00143	0.872	0.00143	1.00000
48	GO:0042281	dolichyl pyrophosphate Man9GlcNAc2 alpha...	7	6	1.77	90	0.00143	0.872	0.00143	0.00143
49	GO:0042283	dolichyl pyrophosphate Glc1Man9GlcNAc2 a...	7	6	1.77	91	0.00143	0.872	0.00143	0.00143
50	GO:0046920	alpha(1,3)-fucosyltransferase activity	7	6	1.77	92	0.00143	0.872	0.00143	0.00143
51	GO:0046921	alpha(1,6)-fucosyltransferase activity	7	6	1.77	93	0.00143	0.872	0.00143	0.00143
52	GO:0019200	carbohydrate kinase activity	34	17	8.60	99	0.00163	0.914	0.00163	0.00163
53	GO:0003743	translation initiation factor activity	26	14	6.58	101	0.00169	0.842	0.00169	0.00169
54	GO:0004683	calmodulin regulated protein kinase acti...	29	15	7.34	104	0.00198	0.769	0.00198	1.00000
55	GO:0008565	protein transporter activity	80	35	20.24	45	0.00023	0.888	0.00200	0.00023
56	GO:0017111	nucleoside-triphosphatase activity	303	122	76.67	12	3.0e-09	0.964	0.00229	1.00000
57	GO:0004437	inositol or phosphatidylinositol phospha...	14	9	3.54	105	0.00233	0.964	0.00233	0.00233
58	GO:0003677	DNA binding	664	204	168.01	53	0.00045	0.423	0.00267	1.00000
59	GO:0030234	enzyme regulator activity	95	49	24.04	16	2.8e-08	0.968	0.00290	0.31814
60	GO:0035004	phosphoinositide 3-kinase activity	25	13	6.33	106	0.00370	0.757	0.00370	0.00370
61	GO:0008094	DNA-dependent ATPase activity	54	23	13.66	108	0.00396	0.967	0.00396	0.02808
62	GO:0005244	voltage-gated ion channel activity	4	4	1.01	109	0.00409	0.998	0.00409	0.00409
63	GO:0005543	phospholipid binding	4	4	1.01	110	0.00409	0.940	0.00409	1.00000
64	GO:0008320	protein carrier activity	4	4	1.01	111	0.00409	0.986	0.00409	1.00000
65	GO:0003777	microtubule motor activity	15	9	3.80	112	0.00452	0.999	0.00452	1.00000
66	GO:0046933	hydrogen ion transporting ATP synthase a...	31	15	7.84	113	0.00454	0.972	0.00454	0.00454
67	GO:0046961	hydrogen ion transporting ATPase activit...	31	15	7.84	114	0.00454	0.972	0.00454	1.00000
68	GO:0000030	mannosyltransferase activity	16	14	4.05	18	3.0e-07	0.993	0.00478	3.0e-07
69	GO:0003887	DNA-directed DNA polymerase activity	24	16	6.07	31	2.3e-05	0.979	0.00478	2.3e-05
70	GO:0016462	pyrophosphatase activity	317	131	80.21	7	9.2e-11	0.985	0.00481	9.5e-07
71	GO:0000810	diacylglycerol pyrophosphate phosphatase...	6	5	1.52	115	0.00489	0.960	0.00489	1.00000
72	GO:0003702	RNA polymerase II transcription factor a...	6	5	1.52	116	0.00489	0.966	0.00489	0.00489
73	GO:0004787	thiamin-pyrophosphatase activity	6	5	1.52	117	0.00489	0.960	0.00489	1.00000
74	GO:0008758	UDP-2,3-diacylglucosamine hydrolase acti...	6	5	1.52	118	0.00489	0.960	0.00489	1.00000
75	GO:0008796	bis(5’-nucleosyl)-tetraphosphatase activ...	6	5	1.52	119	0.00489	0.960	0.00489	0.00489
76	GO:0008828	dATP pyrophosphohydrolase activity	6	5	1.52	120	0.00489	0.960	0.00489	1.00000
77	GO:0016778	diphosphotransferase activity	6	5	1.52	121	0.00489	0.994	0.00489	0.00489
78	GO:0019176	dihydroneopterin monophosphate phosphata...	6	5	1.52	122	0.00489	0.960	0.00489	0.00489

79	GO:0019177	dihydroneopterin triphosphate pyrophosph...	6	5	1.52	123	0.00489	0.960	0.00489	1.00000
80	GO:0019201	nucleotide kinase activity	6	5	1.52	124	0.00489	0.976	0.00489	0.00489
81	GO:0051082	unfolded protein binding	40	18	10.12	126	0.00518	0.891	0.00518	1.00000
82	GO:0008047	enzyme activator activity	26	13	6.58	127	0.00571	0.791	0.00571	1.00000
83	GO:0008408	3’-5’ exonuclease activity	13	8	3.29	128	0.00606	0.988	0.00606	0.00606
84	GO:0003924	GTPase activity	29	14	7.34	129	0.00621	0.966	0.00621	1.00000
85	GO:0004707	MAP kinase activity	27	13	6.83	131	0.00851	0.819	0.00851	0.37152
86	GO:0019207	kinase regulator activity	58	31	14.68	25	3.8e-06	0.796	0.01018	1.00000
87	GO:0019887	protein kinase regulator activity	58	31	14.68	26	3.8e-06	0.796	0.01018	1.00000
88	GO:0004680	casein kinase activity	55	30	13.92	23	3.2e-06	0.658	0.01019	1.00000
89	GO:0004690	cyclic nucleotide-dependent protein kina...	55	30	13.92	24	3.2e-06	0.658	0.01019	1.00000
90	GO:0001565	phorbol ester receptor activity	22	11	5.57	136	0.01082	0.820	0.01082	1.00000
91	GO:0004675	transmembrane receptor protein serine/th...	22	11	5.57	137	0.01082	0.820	0.01082	0.01082
92	GO:0004676	3-phosphoinositide-dependent protein kin...	22	11	5.57	138	0.01082	0.820	0.01082	1.00000
93	GO:0004677	DNA-dependent protein kinase activity	22	11	5.57	139	0.01082	0.820	0.01082	1.00000
94	GO:0004679	AMP-activated protein kinase activity	22	11	5.57	140	0.01082	0.820	0.01082	1.00000
95	GO:0004681	casein kinase I activity	22	11	5.57	141	0.01082	0.820	0.01082	1.00000
96	GO:0004686	eukaryotic elongation factor-2 kinase ac...	22	11	5.57	142	0.01082	0.820	0.01082	1.00000
97	GO:0004688	multifunctional calcium- and calmodulin-...	22	11	5.57	143	0.01082	0.820	0.01082	1.00000
98	GO:0004689	phosphorylase kinase activity	22	11	5.57	144	0.01082	0.820	0.01082	1.00000
99	GO:0004692	cGMP-dependent protein kinase activity	22	11	5.57	145	0.01082	0.820	0.01082	1.00000
100	GO:0004694	eukaryotic translation initiation factor...	22	11	5.57	146	0.01082	0.820	0.01082	1.00000
101	GO:0004695	galactosyltransferase-associated kinase ...	22	11	5.57	147	0.01082	0.820	0.01082	1.00000
102	GO:0004696	glycogen synthase kinase 3 activity	22	11	5.57	148	0.01082	0.820	0.01082	1.00000
103	GO:0004697	protein kinase C activity	22	11	5.57	149	0.01082	0.820	0.01082	1.00000
104	GO:0004698	calcium-dependent protein kinase C activ...	22	11	5.57	150	0.01082	0.820	0.01082	0.01082
105	GO:0004700	atypical protein kinase C activity	22	11	5.57	151	0.01082	0.820	0.01082	0.01082
106	GO:0004701	diacylglycerol-activated phospholipid-de...	22	11	5.57	152	0.01082	0.820	0.01082	0.01082
107	GO:0004703	G-protein coupled receptor kinase activi...	22	11	5.57	153	0.01082	0.820	0.01082	1.00000
108	GO:0004704	NF-kappaB-inducing kinase activity	22	11	5.57	154	0.01082	0.820	0.01082	0.01082
109	GO:0004705	JUN kinase activity	22	11	5.57	155	0.01082	0.820	0.01082	0.01082
110	GO:0004706	JUN kinase kinase kinase activity	22	11	5.57	156	0.01082	0.820	0.01082	0.01082
111	GO:0004708	MAP kinase kinase activity	22	11	5.57	157	0.01082	0.820	0.01082	1.00000
112	GO:0004709	MAP kinase kinase kinase activity	22	11	5.57	158	0.01082	0.820	0.01082	1.00000
113	GO:0004710	MAP/ERK kinase kinase activity	22	11	5.57	159	0.01082	0.820	0.01082	0.01082
114	GO:0004711	ribosomal protein S6 kinase activity	22	11	5.57	160	0.01082	0.820	0.01082	1.00000
115	GO:0004712	protein threonine/tyrosine kinase activi...	22	11	5.57	161	0.01082	0.820	0.01082	1.00000
116	GO:0004714	transmembrane receptor protein tyrosine ...	22	11	5.57	162	0.01082	0.820	0.01082	1.00000
117	GO:0004715	non-membrane spanning protein tyrosine k...	22	11	5.57	163	0.01082	0.820	0.01082	1.00000
118	GO:0004716	receptor signaling protein tyrosine kina...	22	11	5.57	164	0.01082	0.820	0.01082	1.00000
119	GO:0004718	Janus kinase activity	22	11	5.57	165	0.01082	0.820	0.01082	0.01082
120	GO:0008338	MAP kinase 1 activity	22	11	5.57	166	0.01082	0.820	0.01082	0.01082
121	GO:0008339	MP kinase activity	22	11	5.57	167	0.01082	0.820	0.01082	0.01082
122	GO:0008349	MAP kinase kinase kinase kinase activity	22	11	5.57	168	0.01082	0.820	0.01082	0.01082
123	GO:0008384	IkappaB kinase activity	22	11	5.57	169	0.01082	0.820	0.01082	1.00000
124	GO:0008545	JUN kinase kinase activity	22	11	5.57	170	0.01082	0.820	0.01082	0.01082
125	GO:0008607	phosphorylase kinase regulator activity	22	11	5.57	171	0.01082	0.820	0.01082	0.01082
126	GO:0008819	cobinamide kinase activity	22	11	5.57	172	0.01082	0.820	0.01082	0.01082
127	GO:0016538	cyclin-dependent protein kinase regulato...	22	11	5.57	173	0.01082	0.820	0.01082	0.01082
128	GO:0016908	MAP kinase 2 activity	22	11	5.57	174	0.01082	0.820	0.01082	0.01082
129	GO:0016909	SAP kinase activity	22	11	5.57	175	0.01082	0.820	0.01082	1.00000
130	GO:0018720	phenol kinase activity	22	11	5.57	176	0.01082	0.820	0.01082	0.01082
131	GO:0019199	transmembrane receptor protein kinase ac...	22	11	5.57	177	0.01082	0.820	0.01082	1.00000

132	GO:0019209	kinase activator activity	22	11	5.57	178	0.01082	0.820	0.01082	1.00000
133	GO:0019912	cyclin-dependent protein kinase activati...	22	11	5.57	179	0.01082	0.820	0.01082	0.01082
134	GO:0019914	cyclin-dependent protein kinase activati...	22	11	5.57	180	0.01082	0.820	0.01082	0.01082
135	GO:0030295	protein kinase activator activity	22	11	5.57	181	0.01082	0.820	0.01082	1.00000
136	GO:0042556	eukaryotic elongation factor-2 kinase re...	22	11	5.57	182	0.01082	0.820	0.01082	1.00000
137	GO:0042557	eukaryotic elongation factor-2 kinase ac...	22	11	5.57	183	0.01082	0.820	0.01082	0.01082
138	GO:0030695	GTPase regulator activity	14	8	3.54	184	0.01103	0.888	0.01103	0.44101
139	GO:0004308	exo-alpha-sialidase activity	31	14	7.84	185	0.01263	0.218	0.01263	0.01263
140	GO:0004721	phosphoprotein phosphatase activity	31	14	7.84	186	0.01263	0.971	0.01263	0.15323
141	GO:0016997	alpha-sialidase activity	31	14	7.84	187	0.01263	0.218	0.01263	0.44055
142	GO:0042625	ATPase activity, coupled to transmembran...	97	40	24.54	49	0.00038	0.950	0.01476	0.00038
143	GO:0008092	cytoskeletal protein binding	20	10	5.06	192	0.01495	0.998	0.01495	1.00000
144	GO:0008234	cysteine-type peptidase activity	69	26	17.46	193	0.01501	0.934	0.01501	0.15226
145	GO:0004693	cyclin-dependent protein kinase activity	23	11	5.82	195	0.01608	0.810	0.01608	1.00000
146	GO:0008443	phosphofructokinase activity	23	11	5.82	196	0.01608	0.773	0.01608	1.00000
147	GO:0004377	glycolipid 2-alpha-mannosyltransferase a...	3	3	0.76	197	0.01617	0.999	0.01617	1.00000
148	GO:0004605	phosphatidate cytidylyltransferase activ...	3	3	0.76	198	0.01617	0.959	0.01617	0.01617
149	GO:0004749	ribose phosphate diphosphokinase activit...	3	3	0.76	199	0.01617	0.997	0.01617	1.00000
150	GO:0005247	voltage-gated chloride channel activity	3	3	0.76	200	0.01617	0.998	0.01617	1.00000
151	GO:0005254	chloride channel activity	3	3	0.76	201	0.01617	0.998	0.01617	1.00000
152	GO:0016979	lipoate-protein ligase activity	3	3	0.76	202	0.01617	0.997	0.01617	0.01617
153	GO:0004239	methionyl aminopeptidase activity	5	4	1.27	203	0.01630	0.982	0.01630	1.00000
154	GO:0031072	heat shock protein binding	29	13	7.34	204	0.01719	0.971	0.01719	1.00000
155	GO:0004339	glucan 1,4-alpha-glucosidase activity	32	14	8.10	207	0.01734	0.790	0.01734	0.01734
156	GO:0016645	oxidoreductase activity, acting on the C...	18	9	4.55	211	0.02074	0.941	0.02074	0.70509
157	GO:0015399	primary active transporter activity	102	41	25.81	55	0.00061	0.961	0.02075	0.46698
158	GO:0015405	P-P-bond-hydrolysis-driven transporter a...	102	41	25.81	56	0.00061	0.961	0.02075	0.00061
159	GO:0004221	ubiquitin thiolesterase activity	21	10	5.31	213	0.02219	0.892	0.02219	0.02219
160	GO:0004843	ubiquitin-specific protease activity	21	10	5.31	214	0.02219	0.892	0.02219	0.44094
161	GO:0019783	small conjugating protein-specific prote...	21	10	5.31	215	0.02219	0.892	0.02219	1.00000
162	GO:0016790	thiolester hydrolase activity	27	12	6.83	217	0.02343	0.616	0.02343	0.86911
163	GO:0042578	phosphoric ester hydrolase activity	89	36	22.52	72	0.00113	0.964	0.02389	0.70299
164	GO:0004722	protein serine/threonine phosphatase act...	13	7	3.29	218	0.02576	0.877	0.02576	1.00000
165	GO:0019208	phosphatase regulator activity	13	7	3.29	219	0.02576	0.877	0.02576	1.00000
166	GO:0019888	protein phosphatase regulator activity	13	7	3.29	220	0.02576	0.877	0.02576	0.02576
167	GO:0003724	RNA helicase activity	43	17	10.88	222	0.02770	0.727	0.02770	0.02770
168	GO:0008233	peptidase activity	278	100	70.34	35	3.3e-05	0.904	0.02804	0.90812
169	GO:0016779	nucleotidyltransferase activity	77	36	19.48	36	3.4e-05	0.960	0.02809	0.48893
170	GO:0003774	motor activity	23	14	5.82	48	0.00031	0.999	0.02818	0.00031
171	GO:0000175	3’-5’-exoribonuclease activity	8	5	2.02	223	0.02862	0.846	0.02862	1.00000
172	GO:0016776	phosphotransferase activity, phosphate g...	8	5	2.02	224	0.02862	0.976	0.02862	0.02862
173	GO:0003779	actin binding	19	9	4.81	225	0.03074	0.996	0.03074	0.26583
174	GO:0016307	phosphatidylinositol phosphate kinase ac...	25	11	6.33	227	0.03196	0.757	0.03196	0.03196
175	GO:0003678	DNA helicase activity	47	18	11.89	228	0.03324	0.741	0.03324	1.00000
176	GO:0004003	ATP-dependent DNA helicase activity	47	18	11.89	229	0.03324	0.741	0.03324	1.00000
177	GO:0003847	1-alkyl-2-acetylglycerophosphocholine es...	11	6	2.78	230	0.03616	0.919	0.03616	0.03616
178	GO:0004532	exoribonuclease activity	11	6	2.78	231	0.03616	0.795	0.03616	1.00000
179	GO:0008374	O-acyltransferase activity	11	6	2.78	232	0.03616	0.825	0.03616	0.03616
180	GO:0016896	exoribonuclease activity, producing 5’-p...	11	6	2.78	233	0.03616	0.795	0.03616	0.44134
181	GO:0016772	transferase activity, transferring phosp...	393	161	99.44	4	1.2e-12	0.999	0.03618	0.92320
182	GO:0030693	caspase activity	6	4	1.52	234	0.03913	0.732	0.03913	0.03913
183	GO:0016791	phosphoric monoester hydrolase activity	69	29	17.46	100	0.00166	0.972	0.04297	0.73995
184	GO:0004177	aminopeptidase activity	23	10	5.82	237	0.04367	0.353	0.04367	1.00000

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185 GO:0004872                          receptor activity        55          20    13.92             238 0.04459 0.061 0.04459 0.80760
186 GO:0004004         ATP-dependent RNA helicase activity        42          16    10.63             239 0.04541 0.677 0.04541 1.00000
187 GO:0008186               RNA-dependent ATPase activity        42          16    10.63             240 0.04541 0.677 0.04541 0.76601
188 GO:0015462        protein-transporting ATPase activity        42          16    10.63             241 0.04541 0.677 0.04541 1.00000
189 GO:0015616                   DNA translocase activity        42          16    10.63             242 0.04541 0.677 0.04541 1.00000
190 GO:0017116 single-stranded DNA-dependent ATP-depend...        42          16    10.63             243 0.04541 0.677 0.04541 0.56039
191 GO:0042624                  ATPase activity, uncoupled        42          16    10.63             244 0.04541 0.677 0.04541 0.04541
192 GO:0043142 single-stranded DNA-dependent ATPase act...        42          16    10.63             245 0.04541 0.677 0.04541 1.00000

> ##########  Cellular component  #############

         GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS    elim  weight
1   GO:0005839 proteasome core complex (sensu Eukaryota...        13          12     3.70               9 2.5e-06 0.9626 2.5e-06  1.0000
2   GO:0030125                        clathrin vesicle coat        11          10     3.13              17 2.7e-05 0.9997 2.7e-05 2.7e-05
3   GO:0005956                  protein kinase CK2 complex        34          20     9.67              37 0.00019 0.8371 0.00019  1.0000
4   GO:0044430                       cytoskeletal part        34          20     9.67              38 0.00019 0.9883 0.00019  1.0000
5   GO:0043234                         protein complex       475         189   135.13               5 1.3e-09 0.9873 0.00040 3.1e-07
6   GO:0044428                           nuclear part        59          36    16.78               6 1.3e-07 0.9772 0.00054  1.0000
7   GO:0005952       cAMP-dependent protein kinase complex        35          19     9.96              43 0.00107 0.6333 0.00107  1.0000
8   GO:0012505                      endomembrane system        44          29    12.52               7 2.1e-07 0.9987 0.00137  0.2776
9   GO:0005667               transcription factor complex         9           7     2.56              47 0.00301 0.9880 0.00301  1.0000
10  GO:0043231      intracellular membrane-bound organelle       824         280   234.41              10 8.3e-06 0.0987 0.00416  0.1955
11  GO:0000785                             chromatin        23          13     6.54              49 0.00422 0.7251 0.00422  1.0000
12  GO:0005732 small nucleolar ribonucleoprotein comple...        16          10     4.55              50 0.00456 0.7795 0.00456  0.0046
13  GO:0031090                      organelle membrane        88          44    25.03              14 1.1e-05 0.9921 0.00498  1.0000
14  GO:0015630                microtubule cytoskeleton        26          14     7.40              51 0.00541 0.9747 0.00541  1.0000
15  GO:0044424                      intracellular part      1244         431   353.90               4 5.5e-13 0.9251 0.00620  1.0000
16  GO:0005622                           intracellular      1314         455   373.81               1 1.8e-14 0.9425 0.00644  0.5143
17  GO:0000139                         Golgi membrane        10           7     2.84              52 0.00759 0.7083 0.00759  1.0000
18  GO:0005663           DNA replication factor C complex         8           6     2.28              54 0.00840 0.8778 0.00840  1.0000
19  GO:0005875             microtubule associated complex        15           9     4.27              55 0.01033 0.9978 0.01033  1.0000
20  GO:0005783                     endoplasmic reticulum        25          13     7.11              56 0.01063 0.9575 0.01063  1.0000
21  GO:0005789            endoplasmic reticulum membrane        13           8     3.70              57 0.01282 0.9778 0.01282  0.0796
22  GO:0042175 nuclear envelope-endoplasmic reticulum n...        13           8     3.70              58 0.01282 0.9778 0.01282  1.0000
23  GO:0044432              endoplasmic reticulum part        13           8     3.70              59 0.01282 0.9778 0.01282  1.0000
24  GO:0000151                ubiquitin ligase complex        57          24    16.22              61 0.01753 0.9838 0.01753  1.0000
25  GO:0015629                      actin cytoskeleton         9           6     2.56              62 0.01918 0.9996 0.01918  1.0000
26  GO:0005794                         Golgi apparatus        17          12     4.84              39 0.00036 0.8364 0.02204  0.0074
27  GO:0008287 protein serine/threonine phosphatase com...        14           8     3.98              65 0.02258 0.7904 0.02258  1.0000
28  GO:0005798                 Golgi-associated vesicle         7           5     1.99              66 0.02266 0.7694 0.02266  1.0000
29  GO:0000145                               exocyst         3           3     0.85              67 0.02295 0.9994 0.02295  1.0000
30  GO:0005795                            Golgi stack         3           3     0.85              68 0.02295 0.9927 0.02295  1.0000
31  GO:0005938                            cell cortex         3           3     0.85              69 0.02295 0.9994 0.02295  1.0000
32  GO:0012510 trans-Golgi network transport vesicle me...         3           3     0.85              70 0.02295 0.8939 0.02295  1.0000
33  GO:0030130 clathrin coat of trans-Golgi network ves...         3           3     0.85              71 0.02295 0.8939 0.02295  1.0000
34  GO:0030140       trans-Golgi network transport vesicle         3           3     0.85              72 0.02295 0.8939 0.02295  1.0000
35  GO:0044448                       cell cortex part         3           3     0.85              73 0.02295 0.9994 0.02295  1.0000
36  GO:0016459                         myosin complex         5           4     1.42              74 0.02516 0.9998 0.02516  1.0000
37  GO:0005623                                   cell      2281         657   648.91              44 0.00141 0.7033 0.02715  0.0345
38  GO:0044464                              cell part      2281         657   648.91              45 0.00141 0.7033 0.02715  0.0141
39  GO:0016469 proton-transporting two-sector ATPase co...        34          15     9.67              75 0.03587 0.9361 0.03587  1.0000
40  GO:0005635                       nuclear envelope        15           8     4.27              76 0.03658 0.9382 0.03658  1.0000
41  GO:0005643                           nuclear pore        15           8     4.27              77 0.03658 0.9382 0.03658  1.0000
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42	GO:0031965	nuclear membrane	15	8	4.27	78	0.03658	0.9382	0.03658	1.0000	
43	GO:0044453	nuclear membrane part	15	8	4.27	79	0.03658	0.9382	0.03658	1.0000	
44	GO:0046930	pore complex	15	8	4.27	80	0.03658	0.9382	0.03658	1.0000	
45	GO:0005694	chromosome	44	26	12.52	15	1.8e-05	0.8604	0.04361	7.7e-05	

> ########## Biological process #############

	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0006886	intracellular protein transport	82	47	20.40	19	2.8e-10	1.00	2.8e-10	1.00000
2	GO:0007264	small GTPase mediated signal transductio...	40	28	9.95	21	2.1e-09	0.98	2.1e-09	1.00000
3	GO:0006511	ubiquitin-dependent protein catabolic pr...	36	23	8.96	30	7.8e-07	0.99	7.8e-07	7.8e-07
4	GO:0006486	protein amino acid glycosylation	16	13	3.98	39	3.4e-06	1.00	3.4e-06	1.00000
5	GO:0006260	DNA replication	57	35	14.18	22	4.5e-09	0.96	2.2e-05	1.00000
6	GO:0006397	mRNA processing	26	16	6.47	53	7.7e-05	0.96	7.7e-05	7.7e-05
7	GO:0007242	intracellular signaling cascade	74	47	18.41	16	1.6e-12	0.96	8.3e-05	1.6e-12
8	GO:0006468	protein amino acid phosphorylation	198	73	49.27	54	8.6e-05	1.00	8.6e-05	1.00000
9	GO:0015031	protein transport	107	62	26.62	10	1.8e-13	1.00	0.00015	3.0e-13
10	GO:0016192	vesicle-mediated transport	23	16	5.72	42	7.8e-06	1.00	0.00031	2.2e-05
11	GO:0030163	protein catabolic process	44	30	10.95	20	1.5e-09	1.00	0.00034	1.00000
12	GO:0006352	transcription initiation	12	9	2.99	62	0.00037	0.99	0.00037	1.00000
13	GO:0006464	protein modification	368	153	91.56	9	1.6e-13	1.00	0.00057	0.18956
14	GO:0006512	ubiquitin cycle	91	40	22.64	51	4.7e-05	0.98	0.00088	1.00000
15	GO:0006457	protein folding	56	25	13.93	68	0.00093	0.93	0.00093	1.00000
16	GO:0006333	chromatin assembly or disassembly	25	16	6.22	50	3.8e-05	0.99	0.00126	0.00044
17	GO:0000160	two-component signal transduction system...	21	12	5.23	71	0.00157	1.00	0.00157	0.00157
18	GO:0007018	microtubule-based movement	19	11	4.73	74	0.00215	0.95	0.00215	1.00000
19	GO:0006261	DNA-dependent DNA replication	23	15	5.72	52	4.9e-05	0.98	0.00259	1.00000
20	GO:0045045	secretory pathway	22	12	5.47	79	0.00269	1.00	0.00269	0.24756
21	GO:0006461	protein complex assembly	17	10	4.23	80	0.00293	0.98	0.00293	1.00000
22	GO:0006413	translational initiation	25	13	6.22	81	0.00314	0.82	0.00314	0.00314
23	GO:0006534	cysteine metabolic process	4	4	1.00	85	0.00382	0.99	0.00382	0.06171
24	GO:0007067	mitosis	6	5	1.49	87	0.00451	0.97	0.00451	0.04986
25	GO:0043087	regulation of GTPase activity	6	5	1.49	88	0.00451	0.97	0.00451	1.00000
26	GO:0031497	chromatin assembly	18	10	4.48	90	0.00514	1.00	0.00514	1.00000
27	GO:0007010	cytoskeleton organization and biogenesis	32	19	7.96	49	3.3e-05	0.98	0.00522	0.57224
28	GO:0015986	ATP synthesis coupled proton transport	32	15	7.96	91	0.00553	0.97	0.00553	0.00553
29	GO:0044238	primary metabolic process	2361	735	587.45	3	4.9e-24	1.00	0.00607	0.99891
30	GO:0006281	DNA repair	74	35	18.41	45	2.1e-05	0.98	0.00659	1.00000
31	GO:0006298	mismatch repair	11	7	2.74	98	0.00729	0.86	0.00729	1.00000
32	GO:0043283	biopolymer metabolic process	1100	415	273.70	1	4.8e-28	0.99	0.00816	0.42507
33	GO:0006508	proteolysis	271	97	67.43	48	2.4e-05	0.83	0.00825	1.00000
34	GO:0016567	protein ubiquitination	55	22	13.68	102	0.00925	0.98	0.00925	1.00000
35	GO:0006289	nucleotide-excision repair	9	6	2.24	104	0.00968	1.00	0.00968	1.00000
36	GO:0048193	Golgi vesicle transport	9	6	2.24	105	0.00968	0.99	0.00968	1.00000
37	GO:0006769	nicotinamide metabolic process	14	8	3.48	106	0.00990	0.91	0.00990	1.00000
38	GO:0006812	cation transport	108	43	26.87	64	0.00038	0.99	0.01199	0.05486
39	GO:0050789	regulation of biological process	456	134	113.46	116	0.01201	0.70	0.01201	0.41160
40	GO:0006270	DNA replication initiation	7	5	1.74	117	0.01255	0.99	0.01255	1.00000
41	GO:0030029	actin filament-based process	7	5	1.74	118	0.01255	0.99	0.01255	1.00000
42	GO:0030036	actin cytoskeleton organization and biog...	7	5	1.74	119	0.01255	0.99	0.01255	0.15437
43	GO:0008654	phospholipid biosynthetic process	20	10	4.98	124	0.01322	0.89	0.01322	0.03687
44	GO:0046467	membrane lipid biosynthetic process	20	10	4.98	125	0.01322	0.89	0.01322	1.00000
45	GO:0048519	negative regulation of biological proces...	12	7	2.99	126	0.01377	1.00	0.01377	0.43462

46	GO:0006367	transcription initiation from RNA polyme...	5	4	1.24	128	0.01530	0.92	0.01530	1.00000
47	GO:0008380	RNA splicing	5	4	1.24	129	0.01530	1.00	0.01530	1.00000
48	GO:0006493	protein amino acid O-linked glycosylatio...	3	3	0.75	130	0.01537	1.00	0.01537	1.00000
49	GO:0006821	chloride transport	3	3	0.75	131	0.01537	1.00	0.01537	0.01537
50	GO:0006891	intra-Golgi vesicle-mediated transport	3	3	0.75	132	0.01537	1.00	0.01537	1.00000
51	GO:0006914	autophagy	3	3	0.75	133	0.01537	0.98	0.01537	0.06179
52	GO:0050794	regulation of cellular process	437	128	108.73	134	0.01558	0.71	0.01558	0.24547
53	GO:0009117	nucleotide metabolic process	85	39	21.15	44	1.8e-05	0.78	0.01732	0.38549
54	GO:0006139	nucleobase, nucleoside, nucleotide and n...	908	307	225.92	18	8.5e-12	0.72	0.01748	0.97593
55	GO:0009165	nucleotide biosynthetic process	68	30	16.92	63	0.00038	0.89	0.01858	0.57145
56	GO:0048523	negative regulation of cellular process	10	6	2.49	138	0.01916	1.00	0.01916	1.00000
57	GO:0006098	pentose-phosphate shunt	8	5	1.99	143	0.02664	0.82	0.02664	0.02664
58	GO:0006487	protein amino acid N-linked glycosylatio...	8	5	1.99	144	0.02664	0.99	0.02664	1.00000
59	GO:0006739	NADP metabolic process	8	5	1.99	145	0.02664	0.82	0.02664	1.00000
60	GO:0006740	NADPH regeneration	8	5	1.99	146	0.02664	0.82	0.02664	1.00000
61	GO:0006887	exocytosis	8	5	1.99	147	0.02664	0.96	0.02664	1.00000
62	GO:0016481	negative regulation of transcription	8	5	1.99	148	0.02664	1.00	0.02664	1.00000
63	GO:0051258	protein polymerization	8	5	1.99	149	0.02664	0.99	0.02664	1.00000
64	GO:0007049	cell cycle	34	17	8.46	70	0.00133	0.86	0.02737	0.03629
65	GO:0009116	nucleoside metabolic process	19	9	4.73	150	0.02764	0.25	0.02764	0.07609
66	GO:0065007	biological regulation	501	145	124.66	135	0.01590	0.52	0.03405	0.89140
67	GO:0006996	organelle organization and biogenesis	96	50	23.89	23	6.7e-09	0.99	0.03570	0.86136
68	GO:0006342	chromatin silencing	6	4	1.49	154	0.03688	0.99	0.03688	0.03688
69	GO:0006366	transcription from RNA polymerase II pro...	6	4	1.49	155	0.03688	0.96	0.03688	1.00000
70	GO:0016458	gene silencing	6	4	1.49	156	0.03688	0.99	0.03688	1.00000
71	GO:0031507	heterochromatin formation	6	4	1.49	157	0.03688	0.99	0.03688	1.00000
72	GO:0045814	negative regulation of gene expression, ...	6	4	1.49	158	0.03688	0.99	0.03688	1.00000
73	GO:0045892	negative regulation of transcription, DN...	6	4	1.49	159	0.03688	0.99	0.03688	1.00000
74	GO:0051276	chromosome organization and biogenesis	42	24	10.45	41	7.6e-06	0.99	0.03709	0.02245
75	GO:0009123	nucleoside monophosphate metabolic proce...	17	8	4.23	160	0.03891	0.53	0.03891	1.00000
76	GO:0009124	nucleoside monophosphate biosynthetic pr...	17	8	4.23	161	0.03891	0.53	0.03891	1.00000
77	GO:0009892	negative regulation of metabolic process	9	5	2.24	164	0.04784	1.00	0.04784	1.00000
78	GO:0031324	negative regulation of cellular metaboli...	9	5	2.24	165	0.04784	1.00	0.04784	1.00000
79	GO:0045934	negative regulation of nucleobase, nucle...	9	5	2.24	166	0.04784	1.00	0.04784	1.00000
80	GO:0006396	RNA processing	76	34	18.91	56	0.00011	0.76	0.04826	0.11029
81	GO:0006811	ion transport	127	46	31.60	78	0.00259	0.92	0.04906	0.98894
82	GO:0065003	macromolecule complex assembly	66	38	16.42	25	1.2e-08	0.98	0.04929	4.6e-06

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##############################################
##                                          ##
##               Group K                    ##
##                                          ##
##############################################
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```
> ##########  Metabolic function  #############
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	GO.ID	Term	Annotated	Significant	Expected	Rank in classic	classic	KS	elim	weight
1	GO:0003841	1-acylglycerol-3-phosphate O-acyltransfe...	1	1	0.01	2	0.0094	1.0000	0.0094	0.0094
2	GO:0004651	polynucleotide 5’-phosphatase activity	1	1	0.01	3	0.0094	0.9999	0.0094	0.0094
3	GO:0050051	leukotriene-B4 20-monooxygenase activity	1	1	0.01	4	0.0094	0.9999	0.0094	0.0094
4	GO:0004197	cysteine-type endopeptidase activity	57	3	0.54	6	0.0162	0.8418	0.0162	0.0162
5	GO:0004932	mating-type factor pheromone receptor ac...	2	1	0.02	7	0.0188	0.6542	0.0188	0.0188
6	GO:0009042	valine-pyruvate transaminase activity	2	1	0.02	8	0.0188	0.3746	0.0188	0.0188
7	GO:0016503	pheromone receptor activity	2	1	0.02	9	0.0188	0.6542	0.0188	1.0000

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8  GO:0004497                     monooxygenase activity       241           7     2.27              1  0.0070 0.0081 0.0224 0.1171
9  GO:0008234           cysteine-type peptidase activity        69           3     0.65             12  0.0268 0.6678 0.0268 1.0000
10 GO:0004321           fatty-acyl-CoA synthase activity         3           1     0.03             13  0.0280 0.2139 0.0280 0.0280
11 GO:0004818             glutamate-tRNA ligase activity         3           1     0.03             14  0.0280 0.7286 0.0280 0.0280
12 GO:0004312               fatty-acid synthase activity        31           2     0.29             16  0.0341 0.5280 0.0341 0.0341
13 GO:0005355               glucose transporter activity         4           1     0.04             17  0.0372 0.9807 0.0372 0.0372
14 GO:0008800                    beta-lactamase activity         4           1     0.04             18  0.0372 0.8918 0.0372 0.0372
15 GO:0015145        monosaccharide transporter activity         4           1     0.04             19  0.0372 0.9807 0.0372 1.0000
16 GO:0015149                hexose transporter activity         4           1     0.04             20  0.0372 0.9807 0.0372 1.0000
17 GO:0005507                        copper ion binding        35           2     0.33             22  0.0426 0.7438 0.0426 0.0426
18 GO:0005375            copper ion transporter activity         5           1     0.05             23  0.0463 0.7303 0.0463 0.0463

> ##########  Cellular component  #############

       GO.ID                                  Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0005835               fatty acid synthase complex         5           1     0.04              1   0.040  0.1225 0.040  0.040

> ##########  Biological process  #############

       GO.ID                                  Term Annotated Significant Expected Rank in classic classic     KS   elim weight
1  GO:0008610                lipid biosynthetic process       111           5     0.98              1  0.0027 0.7135 0.0027 0.0084
2  GO:0006633             fatty acid biosynthetic process        64           3     0.57              4  0.0184 0.7130 0.0184 1.0000
3  GO:0016053           organic acid biosynthetic process        65           3     0.57              5  0.0192 0.6884 0.0192 1.0000
4  GO:0046394        carboxylic acid biosynthetic process        65           3     0.57              6  0.0192 0.6884 0.0192 1.0000
5  GO:0006370                             mRNA capping         3           1     0.03              7  0.0263 0.1126 0.0263 0.0263
6  GO:0006424             glutamyl-tRNA aminoacylation         3           1     0.03              8  0.0263 0.6882 0.0263 0.0263
7  GO:0009452                              RNA capping         3           1     0.03              9  0.0263 0.1126 0.0263 1.0000
8  GO:0006118                        electron transport       599          10     5.30             10  0.0321 0.0020 0.0321 0.0321
9  GO:0006631             fatty acid metabolic process        82           3     0.72             11  0.0351 0.7818 0.0351 1.0000

##############################################
##                                          ##
##               Group L                    ##
##                                          ##
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> ##########  Metabolic function  #############

    GO.ID                                  Term Annotated Significant Expected Rank in classic classic    KS    elim  weight
1  GO:0003743      translation initiation factor activity        26           3     0.16              1 0.00052 0.858 0.00052 0.00052
2  GO:0004065                    arylsulfatase activity         1           1     0.01              6 0.00623 1.000 0.00623 0.00623
3  GO:0004517             nitric-oxide synthase activity         1           1     0.01              7 0.00623 1.000 0.00623 0.00623
4  GO:0004612 phosphoenolpyruvate carboxykinase (ATP) ...         1           1     0.01              8 0.00623 1.000 0.00623 0.00623
5  GO:0004654 polyribonucleotide nucleotidyltransferas...         1           1     0.01              9 0.00623 1.000 0.00623 0.00623
6  GO:0001584            rhodopsin-like receptor activity        22           2     0.14             10 0.00805 0.266 0.00805 0.00805
7  GO:0004408          holocytochrome-c synthase activity         2           1     0.01             13 0.01242 0.979 0.01242 0.01242
8  GO:0001668 phosphatidylinositol-4,5-bisphosphate 5-...         3           1     0.02             15 0.01857 1.000 0.01857 0.01857
9  GO:0004086       carbamoyl-phosphate synthase activity         3           1     0.02             16 0.01857 0.670 0.01857 0.01857
10 GO:0008330 protein tyrosine/threonine phosphatase a...         3           1     0.02             17 0.01857 1.000 0.01857 0.01857
11 GO:0008579             JUN kinase phosphatase activity         3           1     0.02             18 0.01857 1.000 0.01857 0.01857
12 GO:0008969       phosphohistidine phosphatase activity         3           1     0.02             19 0.01857 1.000 0.01857 0.01857
13 GO:0016312 inositol bisphosphate phosphatase activi...         3           1     0.02             20 0.01857 1.000 0.01857 0.01857
14 GO:0017017             MAP kinase phosphatase activity         3           1     0.02             21 0.01857 1.000 0.01857 0.01857
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15 GO:0017161 inositol-1,3,4-trisphosphate 4-phosphata...         3           1     0.02              22 0.01857 1.000 0.01857 0.01857
16 GO:0019175    alpha-ribazole-5'-P phosphatase activity         3           1     0.02              23 0.01857 1.000 0.01857 0.01857
17 GO:0019178                     NADP phosphatase activity         3           1     0.02              24 0.01857 1.000 0.01857 0.01857
18 GO:0019198 transmembrane receptor protein phosphata...         3           1     0.02              25 0.01857 1.000 0.01857 0.01857
19 GO:0030351 inositol-1,3,4,5,6-pentakisphosphate 3-p...         3           1     0.02              26 0.01857 1.000 0.01857 0.01857
20 GO:0030352 inositol-1,4,5,6-tetrakisphosphate 6-pho...         3           1     0.02              27 0.01857 1.000 0.01857 0.01857
21 GO:0005525                                 GTP binding        94           3     0.59              29 0.02015 0.888 0.02015 0.02015
22 GO:0019001                   guanyl nucleotide binding        94           3     0.59              30 0.02015 0.888 0.02015 1.00000
23 GO:0004351           glutamate decarboxylase activity         4           1     0.02              31 0.02469 0.980 0.02469 0.02469
24 GO:0008252                      nucleotidase activity         4           1     0.02              32 0.02469 1.000 0.02469 0.02469
25 GO:0042576           aspartyl aminopeptidase activity         4           1     0.02              33 0.02469 0.994 0.02469 0.02469
26 GO:0042577                 lipid phosphatase activity         4           1     0.02              34 0.02469 0.994 0.02469 1.00000
27 GO:0046030 inositol trisphosphate phosphatase activ...         4           1     0.02              35 0.02469 0.994 0.02469 1.00000
28 GO:0015450               protein translocase activity         5           1     0.03              37 0.03076 1.000 0.03076 0.03076
29 GO:0046983             protein dimerization activity         5           1     0.03              38 0.03076 0.784 0.03076 0.03076
30 GO:0016717 oxidoreductase activity, acting on paire...         6           1     0.04              39 0.03681 1.000 0.03681 0.03681

> ##########  Cellular component  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0005744 mitochondrial inner membrane presequence...         1           1     0.01               1  0.0082  0.9999 0.0082 0.0082

> ##########  Biological process  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS    elim  weight
1  GO:0006413                  translational initiation        25           3     0.17               1 0.00062 0.826 0.00062 0.00062
2  GO:0006809          nitric oxide biosynthetic process         1           1     0.01               4 0.00690 1.000 0.00690 0.00690
3  GO:0008283                        cell proliferation         2           1     0.01               8 0.01375 0.962 0.01375 0.01375
4  GO:0007166 cell surface receptor linked signal tran...        30           2     0.21               9 0.01779 0.094 0.01779 1.00000
5  GO:0007186 G-protein coupled receptor protein signa...        30           2     0.21              10 0.01779 0.094 0.01779 0.01779
6  GO:0006090                 pyruvate metabolic process         3           1     0.02              11 0.02056 1.000 0.02056 1.00000
7  GO:0006094                           gluconeogenesis         3           1     0.02              12 0.02056 1.000 0.02056 0.02056
8  GO:0006417                  regulation of translation         3           1     0.02              13 0.02056 0.922 0.02056 1.00000
9  GO:0006446     regulation of translational initiation         3           1     0.02              14 0.02056 0.922 0.02056 1.00000
10 GO:0009889         regulation of biosynthetic process         3           1     0.02              15 0.02056 0.922 0.02056 1.00000
11 GO:0031326 regulation of cellular biosynthetic proc...         3           1     0.02              16 0.02056 0.922 0.02056 1.00000
12 GO:0019319                hexose biosynthetic process         5           1     0.03              18 0.03404 1.000 0.03404 1.00000
13 GO:0019856        pyrimidine base biosynthetic process         5           1     0.03              19 0.03404 0.707 0.03404 0.03404
14 GO:0046165               alcohol biosynthetic process         5           1     0.03              20 0.03404 1.000 0.03404 1.00000
15 GO:0046364         monosaccharide biosynthetic process         5           1     0.03              21 0.03404 1.000 0.03404 1.00000
16 GO:0006636                   fatty acid desaturation         6           1     0.04              22 0.04071 1.000 0.04071 0.04071
17 GO:0006270                 DNA replication initiation         7           1     0.05              23 0.04734 0.998 0.04734 0.04734
18 GO:0051246     regulation of protein metabolic process         7           1     0.05              24 0.04734 1.000 0.04734 1.00000

##############################################
##                                          ##
##               Group M                    ##
##                                          ##
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> ##########  Metabolic function  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS   elim weight
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1  GO:0015109               chromate transporter activity         1           1     0.00               1  0.0032 0.99998 0.0032 0.0032
2  GO:0008171                O-methyltransferase activity        34           2     0.11               2  0.0051 0.49789 0.0051 0.0051
3  GO:0004015 adenosylmethionine-8-amino-7-oxononanoat...         2           1     0.01               3  0.0064 0.95814 0.0064 0.0064
4  GO:0050525                            cutinase activity         3           1     0.01               4  0.0096 0.98407 0.0096 0.0096
5  GO:0005179                             hormone activity         4           1     0.01               5  0.0128 0.81365 0.0128 0.0128
6  GO:0047657          alpha-1,3-glucan synthase activity         4           1     0.01               6  0.0128 0.28965 0.0128 0.0128
7  GO:0005102                             receptor binding         5           1     0.02               7  0.0159 0.88496 0.0159 1.0000
8  GO:0030248                            cellulose binding         8           1     0.03               8  0.0254 0.99996 0.0254 0.0254
9  GO:0018662             phenol 2-monooxygenase activity         9           1     0.03               9  0.0285 0.72391 0.0285 0.0285
10 GO:0000252 C-3 sterol dehydrogenase (C-4 sterol dec...        10           1     0.03              11  0.0316 0.04400 0.0316 0.0316
11 GO:0000253            3-keto sterol reductase activity        10           1     0.03              12  0.0316 0.04400 0.0316 0.0316
12 GO:0004495                mevaldate reductase activity        10           1     0.03              13  0.0316 0.04400 0.0316 0.0316
13 GO:0018451              epoxide dehydrogenase activity        10           1     0.03              14  0.0316 0.04400 0.0316 0.0316
14 GO:0018452 5-exo-hydroxycamphor dehydrogenase activ...        10           1     0.03              15  0.0316 0.04400 0.0316 0.0316
15 GO:0018453 2-hydroxytetrahydrofuran dehydrogenase a...        10           1     0.03              16  0.0316 0.04400 0.0316 0.0316
16 GO:0048258            3-ketoglucose-reductase activity        10           1     0.03              17  0.0316 0.04400 0.0316 0.0316
17 GO:0003910                     DNA ligase (ATP) activity        11           1     0.04              18  0.0347 0.46927 0.0347 0.0347
18 GO:0003909                           DNA ligase activity        12           1     0.04              19  0.0378 0.33790 0.0378 1.0000
19 GO:0030170                 pyridoxal phosphate binding        12           1     0.04              20  0.0378 0.31500 0.0378 0.0378
20 GO:0008875            gluconate dehydrogenase activity        13           1     0.04              21  0.0409 0.08143 0.0409 0.0409
21 GO:0016886 ligase activity, forming phosphoric este...        13           1     0.04              22  0.0409 0.50841 0.0409 1.0000
22 GO:0001871                              pattern binding        15           1     0.05              24  0.0470 0.99992 0.0470 1.0000
23 GO:0004556                     alpha-amylase activity        15           1     0.05              25  0.0470 0.63043 0.0470 0.0470
24 GO:0016160                            amylase activity        15           1     0.05              26  0.0470 0.63043 0.0470 1.0000
25 GO:0030247                     polysaccharide binding        15           1     0.05              27  0.0470 0.99992 0.0470 1.0000

> ##########  Cellular component  #############

       GO.ID                                Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0005576                  extracellular region        25           3     0.09               1   6e-05  1.0000 6e-05  6e-05


> ##########  Biological process  #############

       GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS   elim weight
1  GO:0015703                   chromate transport         1           1     0.00               1  0.0026 1.0000 0.0026 0.0026
2  GO:0006310                    DNA recombination        14           1     0.04               3  0.0357 0.2968 0.0357 0.0357

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##                                          ##
##                Group N                   ##
##                                          ##
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> ##########  Metabolic function  #############

         GO.ID                                      Term Annotated Significant Expected Rank in classic classic   KS    elim  weight
1   GO:0003899        DNA-directed RNA polymerase activity        33          11     2.13               1 3.7e-06 0.95 3.7e-06 3.7e-06
2   GO:0008425 2-polyprenyl-6-methoxy-1,4-benzoquinone ...         8           4     0.52               6 0.00097 0.99 0.00097 0.00097
3   GO:0016423 tRNA (guanine) methyltransferase activit...         8           4     0.52               7 0.00097 0.97 0.00097 0.00097
4   GO:0003723                                 RNA binding        76          13     4.91              10 0.00101 0.87 0.00101 0.00101
5   GO:0004812              aminoacyl-tRNA ligase activity        51          10     3.29              11 0.00131 1.00 0.00131 0.00131
6   GO:0004307     ethanolaminephosphotransferase activity         2           2     0.13              18 0.00416 0.99 0.00416 0.00416
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7	GO:0004534	5’-3’ exoribonuclease activity	6	3	0.39	19	0.00462	0.78	0.00462	0.00462
8	GO:0008565	protein transporter activity	80	12	5.17	21	0.00486	0.97	0.00486	0.00486
9	GO:0005525	GTP binding	94	13	6.07	23	0.00695	0.99	0.00695	0.00695
10	GO:0000179	rRNA (adenine-N6,N6-)-dimethyltransferas...	7	3	0.45	26	0.00769	0.98	0.00769	0.00769
11	GO:0004372	glycine hydroxymethyltransferase activit...	7	3	0.45	27	0.00769	0.82	0.00769	0.00769
12	GO:0004730	pseudouridylate synthase activity	7	3	0.45	28	0.00769	0.60	0.00769	0.00769
13	GO:0008174	mRNA methyltransferase activity	7	3	0.45	29	0.00769	0.98	0.00769	0.00769
14	GO:0008326	site-specific DNA-methyltransferase (cyt...	7	3	0.45	30	0.00769	0.98	0.00769	0.00769
15	GO:0008650	rRNA (uridine-2’-O-)-methyltransferase a...	7	3	0.45	31	0.00769	0.98	0.00769	0.00769
16	GO:0009383	rRNA (cytosine-C5-967)-methyltransferase...	7	3	0.45	32	0.00769	0.98	0.00769	0.00769
17	GO:0016205	selenocysteine methyltransferase activit...	7	3	0.45	33	0.00769	0.98	0.00769	0.00769
18	GO:0016274	protein-arginine N-methyltransferase act...	7	3	0.45	34	0.00769	0.98	0.00769	0.00769
19	GO:0016300	tRNA (uracil) methyltransferase activity	7	3	0.45	35	0.00769	0.98	0.00769	0.00769
20	GO:0016424	tRNA (guanosine) methyltransferase activ...	7	3	0.45	36	0.00769	0.98	0.00769	0.00769
21	GO:0016426	tRNA (adenine)-methyltransferase activit...	7	3	0.45	37	0.00769	0.98	0.00769	0.00769
22	GO:0016427	tRNA (cytosine)-methyltransferase activi...	7	3	0.45	38	0.00769	0.98	0.00769	0.00769
23	GO:0016431	tRNA (uridine) methyltransferase activit...	7	3	0.45	39	0.00769	0.98	0.00769	0.00769
24	GO:0016435	rRNA (guanine) methyltransferase activit...	7	3	0.45	40	0.00769	0.98	0.00769	0.00769
25	GO:0018423	protein-leucine O-methyltransferase acti...	7	3	0.45	41	0.00769	0.98	0.00769	0.00769
26	GO:0018707	1-phenanthrol methyltransferase activity	7	3	0.45	42	0.00769	0.98	0.00769	0.00769
27	GO:0019702	protein-arginine N5-methyltransferase ac...	7	3	0.45	43	0.00769	0.98	0.00769	0.00769
28	GO:0030792	methylarsonite methyltransferase activit...	7	3	0.45	44	0.00769	0.98	0.00769	0.00769
29	GO:0000175	3’-5’-exoribonuclease activity	8	3	0.52	50	0.01172	0.62	0.01172	0.01172
30	GO:0003880	C-terminal protein carboxyl methyltransf...	8	3	0.52	51	0.01172	0.97	0.01172	0.01172
31	GO:0003838	sterol 24-C-methyltransferase activity	3	2	0.19	53	0.01195	0.77	0.01195	0.01195
32	GO:0004826	phenylalanine-tRNA ligase activity	3	2	0.19	54	0.01195	1.00	0.01195	1.00000
33	GO:0008825	cyclopropane-fatty-acyl-phospholipid syn...	3	2	0.19	55	0.01195	1.00	0.01195	0.01195
34	GO:0016814	hydrolase activity, acting on carbon-nit...	15	4	0.97	56	0.01322	1.00	0.01322	1.00000
35	GO:0004840	ubiquitin conjugating enzyme activity	23	5	1.49	57	0.01398	0.96	0.01398	0.01398
36	GO:0008639	small protein conjugating enzyme activit...	23	5	1.49	58	0.01398	0.96	0.01398	1.00000
37	GO:0003676	nucleic acid binding	1047	90	67.63	14	0.00155	0.26	0.01534	0.01306
38	GO:0016278	lysine N-methyltransferase activity	9	3	0.58	59	0.01675	0.92	0.01675	1.00000
39	GO:0016279	protein-lysine N-methyltransferase activ...	9	3	0.58	60	0.01675	0.92	0.01675	0.01675
40	GO:0008169	C-methyltransferase activity	12	6	0.78	3	4.6e-05	0.98	0.02246	1.00000
41	GO:0004000	adenosine deaminase activity	4	2	0.26	61	0.02288	1.00	0.02288	0.02288
42	GO:0008135	translation factor activity, nucleic aci...	36	6	2.33	62	0.02608	0.92	0.02608	1.00000
43	GO:0045182	translation regulator activity	36	6	2.33	63	0.02608	0.92	0.02608	1.00000
44	GO:0008121	ubiquinol-cytochrome-c reductase activit...	5	2	0.32	69	0.03652	1.00	0.03652	0.03652
45	GO:0015450	protein translocase activity	5	2	0.32	70	0.03652	1.00	0.03652	1.00000
46	GO:0016597	amino acid binding	5	2	0.32	71	0.03652	0.57	0.03652	0.03652
47	GO:0016681	oxidoreductase activity, acting on diphe...	5	2	0.32	72	0.03652	1.00	0.03652	1.00000
48	GO:0016742	hydroxymethyl-, formyl- and related tran...	5	2	0.32	73	0.03652	0.73	0.03652	1.00000
49	GO:0043176	amine binding	5	2	0.32	74	0.03652	0.57	0.03652	1.00000
50	GO:0008757	S-adenosylmethionine-dependent methyltra...	103	15	6.65	17	0.00232	0.79	0.03900	0.54721
51	GO:0016741	transferase activity, transferring one-c...	162	23	10.46	4	0.00026	0.78	0.04227	0.57131
52	GO:0008408	3’-5’ exonuclease activity	13	3	0.84	80	0.04708	0.85	0.04708	1.00000
53	GO:0018585	fluorene oxygenase activity	22	4	1.42	82	0.04964	0.28	0.04964	0.04964
54	GO:0018586	mono-butyltin dioxygenase activity	22	4	1.42	83	0.04964	0.28	0.04964	0.04964
55	GO:0018587	limonene 8-monooxygenase activity	22	4	1.42	84	0.04964	0.28	0.04964	0.04964
56	GO:0018588	tri-n-butyltin dioxygenase activity	22	4	1.42	85	0.04964	0.28	0.04964	0.04964
57	GO:0018589	di-n-butyltin dioxygenase activity	22	4	1.42	86	0.04964	0.28	0.04964	0.04964
58	GO:0018590	methylsilanetriol hydroxylase activity	22	4	1.42	87	0.04964	0.28	0.04964	0.04964
59	GO:0018591	methyl tertiary butyl ether 3-monooxygen...	22	4	1.42	88	0.04964	0.28	0.04964	0.04964

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60  GO:0018592    4-nitrocatechol 4-monooxygenase activity        22           4     1.42              89 0.04964 0.28 0.04964 0.04964
61  GO:0018593 4-chlorophenoxyacetate monooxygenase act...        22           4     1.42              90 0.04964 0.28 0.04964 0.04964
62  GO:0018594 tert-butyl alcohol 2-monooxygenase activ...        22           4     1.42              91 0.04964 0.28 0.04964 0.04964
63  GO:0018595         alpha-pinene monooxygenase activity        22           4     1.42              92 0.04964 0.28 0.04964 0.04964
64  GO:0018596     dimethylsilanediol hydroxylase activity        22           4     1.42              93 0.04964 0.28 0.04964 0.04964
65  GO:0018597              ammonia monooxygenase activity        22           4     1.42              94 0.04964 0.28 0.04964 0.04964
66  GO:0018598 hydroxymethylsilanetriol oxidase activit...        22           4     1.42              95 0.04964 0.28 0.04964 0.04964
67  GO:0018599 2-hydroxyisobutyrate 3-monooxygenase act...        22           4     1.42              96 0.04964 0.28 0.04964 0.04964
68  GO:0018600         alpha-pinene dehydrogenase activity        22           4     1.42              97 0.04964 0.28 0.04964 0.04964
69  GO:0018601      4-nitrophenol 2-monooxygenase activity        22           4     1.42              98 0.04964 0.28 0.04964 0.04964

> ##########  Cellular component  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS   elim weight
1  GO:0005741               mitochondrial outer membrane         5           3     0.31               6 0.00209 1.0000 0.0021 0.0021
2  GO:0044428                            nuclear part        59          10     3.64               9 0.00266 0.9768 0.0027 1.0000
3  GO:0005737                               cytoplasm       418          40    25.76               4 0.00163 0.9988 0.0058 0.1638
4  GO:0031981                             nuclear lumen        34           6     2.10              14 0.01580 0.9932 0.0158 1.0000
5  GO:0043234                          protein complex       475          40    29.28              15 0.01667 0.1111 0.0167 0.9378
6  GO:0030529                 ribonucleoprotein complex       163          17    10.05              16 0.01980 0.9947 0.0198 0.0661
7  GO:0031090                       organelle membrane        88          13     5.42               8 0.00231 0.4633 0.0257 1.0000
8  GO:0044444                        cytoplasmic part       305          29    18.80              11 0.00902 0.9995 0.0323 1.0000
9  GO:0005677                chromatin silencing complex         6           2     0.37              23 0.04804 0.9942 0.0480 0.0480
10 GO:0016585               chromatin remodeling complex         6           2     0.37              24 0.04804 0.9942 0.0480 1.0000

> ##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic   KS   elim  weight
1  GO:0006418 tRNA aminoacylation for protein translat...        50          10     3.27              13 0.00120 0.98 0.0012 1.00000
2  GO:0008033                           tRNA processing        14           5     0.91              17 0.00141 0.88 0.0014 1.00000
3  GO:0006396                            RNA processing        76          16     4.97               1 2.2e-05 0.34 0.0017 5.3e-05
4  GO:0016043            cell organization and biogenesis       220          26    14.37              19 0.00204 1.00 0.0020 1.00000
5  GO:0016071                      mRNA metabolic process        32           7     2.09              20 0.00386 0.99 0.0039 0.00386
6  GO:0015940           pantothenate biosynthetic process         2           2     0.13              22 0.00425 1.00 0.0043 0.00425
7  GO:0044237                 cellular metabolic process      2857         218   186.65               4 6.2e-05 0.14 0.0051 0.60508
8  GO:0009058                      biosynthetic process       703          72    45.93               3 3.0e-05 0.99 0.0053 0.23068
9  GO:0006643            membrane lipid metabolic process        32           9     2.09               6 0.00014 0.95 0.0056 1.00000
10 GO:0008654           phospholipid biosynthetic process        20           5     1.31              25 0.00790 0.91 0.0079 1.00000
11 GO:0015031                         protein transport       107          14     6.99              27 0.00918 1.00 0.0092 0.04343
12 GO:0009126 purine nucleoside monophosphate metaboli...        14           4     0.91              28 0.01059 0.18 0.0106 1.00000
13 GO:0009127 purine nucleoside monophosphate biosynth...        14           4     0.91              29 0.01059 0.18 0.0106 1.00000
14 GO:0009167 purine ribonucleoside monophosphate meta...        14           4     0.91              30 0.01059 0.18 0.0106 1.00000
15 GO:0009168 purine ribonucleoside monophosphate bios...        14           4     0.91              31 0.01059 0.18 0.0106 0.11191
16 GO:0006644              phospholipid metabolic process        28           8     1.83               8 0.00030 0.94 0.0117 0.00220
17 GO:0006338                      chromatin remodeling         8           3     0.52              32 0.01208 0.99 0.0121 0.12576
18 GO:0006122 mitochondrial electron transport, ubiqui...         3           2     0.20              33 0.01221 1.00 0.0122 0.01221
19 GO:0006207 'de novo' pyrimidine base biosynthetic p...         3           2     0.20              34 0.01221 0.99 0.0122 0.01221
20 GO:0006432            phenylalanyl-tRNA aminoacylation         3           2     0.20              35 0.01221 1.00 0.0122 1.00000
21 GO:0006743                ubiquinone metabolic process         3           2     0.20              36 0.01221 0.99 0.0122 1.00000
22 GO:0006744             ubiquinone biosynthetic process         3           2     0.20              37 0.01221 0.99 0.0122 0.01221
23 GO:0042375          quinone cofactor metabolic process         3           2     0.20              38 0.01221 0.99 0.0122 1.00000
24 GO:0045426       quinone cofactor biosynthetic process         3           2     0.20              39 0.01221 0.99 0.0122 1.00000
25 GO:0009156 ribonucleoside monophosphate biosyntheti...        16           4     1.05              42 0.01736 0.24 0.0174 1.00000
```

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26 GO:0009161 ribonucleoside monophosphate metabolic p...        16          4     1.05              43 0.01736 0.24 0.0174 1.00000
27 GO:0009123 nucleoside monophosphate metabolic proce...        17          4     1.11              44 0.02157 0.27 0.0216 1.00000
28 GO:0009124 nucleoside monophosphate biosynthetic pr...        17          4     1.11              45 0.02157 0.27 0.0216 1.00000
29 GO:0007001 chromosome organization and biogenesis (...        35          6     2.29              46 0.02403 0.83 0.0240 0.52062
30 GO:0006397                              mRNA processing        26          5     1.70              47 0.02431 0.97 0.0243 1.00000
31 GO:0031497                            chromatin assembly       18          4     1.18              48 0.02634 0.99 0.0263 0.18096
32 GO:0022613 ribonucleoprotein complex biogenesis and...        36          6     2.35              49 0.02731 0.91 0.0273 0.33059
33 GO:0044238                    primary metabolic process      2361        183   154.24               9 0.00038 0.35 0.0302 0.94848
34 GO:0016568                       chromatin modification        11          3     0.72              51 0.03076 0.99 0.0308 1.00000
35 GO:0006188                     IMP biosynthetic process         5          2     0.33              53 0.03729 0.25 0.0373 1.00000
36 GO:0006189          'de novo' IMP biosynthetic process         5          2     0.33              54 0.03729 0.25 0.0373 0.03729
37 GO:0006505                GPI anchor metabolic process         5          2     0.33              55 0.03729 1.00 0.0373 1.00000
38 GO:0006506              GPI anchor biosynthetic process        5          2     0.33              56 0.03729 1.00 0.0373 0.03729
39 GO:0019856        pyrimidine base biosynthetic process         5          2     0.33              57 0.03729 0.99 0.0373 1.00000
40 GO:0030384          phosphoinositide metabolic process         5          2     0.33              58 0.03729 1.00 0.0373 1.00000
41 GO:0046040                      IMP metabolic process          5          2     0.33              59 0.03729 0.25 0.0373 1.00000
42 GO:0046489       phosphoinositide biosynthetic process         5          2     0.33              60 0.03729 1.00 0.0373 1.00000
43 GO:0006412                                translation       231         28    15.09              12 0.00093 1.00 0.0388 0.00093
44 GO:0006206           pyrimidine base metabolic process        12          3     0.78              61 0.03907 0.97 0.0391 0.45384
45 GO:0006886             intracellular protein transport        82         10     5.36              62 0.03955 1.00 0.0396 1.00000
46 GO:0006323                              DNA packaging         30          5     1.96              63 0.04261 0.92 0.0426 1.00000
47 GO:0006325 establishment and/or maintenance of chro...        30          5     1.96              64 0.04261 0.92 0.0426 1.00000
48 GO:0006996       organelle organization and biogenesis        96         11     6.27              67 0.04698 0.98 0.0470 0.90842
49 GO:0009059          macromolecule biosynthetic process       288         32    18.82              18 0.00180 1.00 0.0485 1.00000

##############################################
##                                          ##
##               Group O                    ##
##                                          ##
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> ##########  Metabolic function  #############

    GO.ID                                     Term Annotated Significant Expected Rank in classic classic      KS    elim weight
1  GO:0004497                    monooxygenase activity       241          13     4.67               2 0.00071 0.03423 0.00071 0.0133
2  GO:0016702 oxidoreductase activity, acting on singl...        16          3     0.31               3 0.00331 0.99941 0.00331 0.0033
3  GO:0015520 tetracycline:hydrogen antiporter activit...        36          4     0.70               5 0.00489 0.93722 0.00489 0.0049
4  GO:0018731 1-oxa-2-oxocycloheptane lactonase activi...         6          2     0.12               9 0.00531 0.60560 0.00531 0.0053
5  GO:0018732             sulfolactone hydrolase activity         6          2     0.12              10 0.00531 0.60560 0.00531 0.0053
6  GO:0018733      3,4-dihydrocoumarin hydrolase activity         6          2     0.12              11 0.00531 0.60560 0.00531 0.0053
7  GO:0018734            butyrolactone hydrolase activity         6          2     0.12              12 0.00531 0.60560 0.00531 0.0053
8  GO:0003834 beta-carotene 15,15'-monooxygenase activ...         1          1     0.02              19 0.01940 0.99960 0.01940 1.0000
9  GO:0004507      steroid 11-beta-monooxygenase activity         1          1     0.02              20 0.01940 0.99965 0.01940 0.0194
10 GO:0004671 protein-S-isoprenylcysteine O-methyltran...        1          1     0.02              21 0.01940 0.99999 0.01940 0.0194
11 GO:0050501                hyaluronan synthase activity        1          1     0.02              22 0.01940 0.99942 0.01940 0.0194
12 GO:0004601                        peroxidase activity        32          3     0.62              23 0.02341 0.93420 0.02341 0.0234
13 GO:0016684 oxidoreductase activity, acting on perox...        32          3     0.62              24 0.02341 0.93420 0.02341 1.0000
14 GO:0046912 transferase activity, transferring acyl ...        13          2     0.25              25 0.02529 0.88471 0.02529 0.0253
15 GO:0016209                       antioxidant activity         34          3     0.66              26 0.02747 0.95037 0.02747 1.0000
16 GO:0004033                aldo-keto reductase activity        16          2     0.31              27 0.03747 0.00133 0.03747 0.0375
17 GO:0004502         kynurenine 3-monooxygenase activity         2          1     0.04              28 0.03842 0.77790 0.03842 0.0384
18 GO:0008395                steroid hydroxylase activity         2          1     0.04              29 0.03842 0.99931 0.03842 1.0000
19 GO:0016713 oxidoreductase activity, acting on paire...        2          1     0.04              30 0.03842 0.82274 0.03842 1.0000
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20 GO:0016491                    oxidoreductase activity      1146          38    22.23               1 0.00028 0.01090 0.04808 0.8477

> ##########  Cellular component  #############

    GO.ID                                Term Annotated Significant Expected Rank in classic classic      KS    elim  weight
1  GO:0016021                 integral to membrane       698          19     9.33               1 0.00029  0.0476 0.00029 0.00029

> ##########  Biological process  #############


    GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS    elim  weight
1  GO:0006118                       electron transport       599          26    11.24               1 2.1e-05 0.009 2.1e-05 2.1e-05
2  GO:0006725       aromatic compound metabolic process       173          10     3.25               3  0.0013 0.024  0.0013  0.0032
3  GO:0015904                    tetracycline transport        36           4     0.68               4  0.0043 0.872  0.0043  0.0043
4  GO:0006479            protein amino acid methylation         1           1     0.02               8  0.0188 1.000  0.0188  1.0000
5  GO:0006481 C-terminal protein amino acid methylatio...         1           1     0.02               9  0.0188 1.000  0.0188  0.0188
6  GO:0008213              protein amino acid alkylation         1           1     0.02              10  0.0188 1.000  0.0188  1.0000
7  GO:0018410 peptide or protein carboxyl-terminal blo...         1           1     0.02              11  0.0188 1.000  0.0188  1.0000

##############################################
##                                          ##
##               Group P                    ##
##                                          ##
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> ##########  Metabolic function  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic    KS    elim weight
1  GO:0005215                       transporter activity       843          14     5.55               1 0.00055 0.994 0.00055 0.0146
2  GO:0004023 alcohol dehydrogenase activity, metal io...        17           2     0.11               2 0.00539 0.658 0.00539 0.0054
3  GO:0004024 alcohol dehydrogenase activity, zinc-dep...        17           2     0.11               3 0.00539 0.658 0.00539 0.0054
4  GO:0004025 alcohol dehydrogenase activity, iron-dep...        17           2     0.11               4 0.00539 0.658 0.00539 0.0054
5  GO:0000049                              tRNA binding         1           1     0.01               6 0.00658 1.000 0.00658 0.0066
6  GO:0005267                potassium channel activity         2           1     0.01               7 0.01313 1.000 0.01313 0.0131
7  GO:0008271                   sulfate porter activity         2           1     0.01               8 0.01313 0.977 0.01313 0.0131
8  GO:0008766 UDP-N-acetylmuramoylalanyl-D-glutamyl-2,...         2           1     0.01               9 0.01313 0.728 0.01313 0.0131
9  GO:0009374                           biotin binding         2           1     0.01              10 0.01313 1.000 0.01313 0.0131
10 GO:0015116              sulfate transporter activity         2           1     0.01              11 0.01313 0.977 0.01313 1.0000
11 GO:0018169 ribosomal S6-glutamic acid ligase activi...         2           1     0.01              12 0.01313 0.728 0.01313 0.0131
12 GO:0019842                          vitamin binding        78           3     0.51              13 0.01424 0.284 0.01424 1.0000
13 GO:0015290 electrochemical potential-driven transpo...       235           5     1.55              14 0.01789 0.865 0.01789 1.0000
14 GO:0015291                          porter activity       235           5     1.55              15 0.01789 0.865 0.01789 0.4117
15 GO:0004357       glutamate-cysteine ligase activity         3           1     0.02              16 0.01962 0.999 0.01962 0.0196
16 GO:0048037                       cofactor binding       160           4     1.05              17 0.02013 0.032 0.02013 0.0512
17 GO:0016881          acid-amino acid ligase activity        90           3     0.59              18 0.02084 0.639 0.02084 1.0000
18 GO:0003984            acetolactate synthase activity         4           1     0.03              19 0.02608 0.768 0.02608 0.0261
19 GO:0008447              L-ascorbate oxidase activity         4           1     0.03              20 0.02608 0.926 0.02608 0.0261
20 GO:0005261                   cation channel activity         5           1     0.03              21 0.03250 1.000 0.03250 1.0000
21 GO:0016597                        amino acid binding         5           1     0.03              22 0.03250 0.693 0.03250 0.0325
22 GO:0016682 oxidoreductase activity, acting on diphe...         5           1     0.03              23 0.03250 0.803 0.03250 1.0000
23 GO:0043176                          amine binding         5           1     0.03              24 0.03250 0.693 0.03250 1.0000
24 GO:0016879 ligase activity, forming carbon-nitrogen...       121           3     0.80              25 0.04449 0.180 0.04449 1.0000
```

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> ##########  Cellular component  #############

       GO.ID                                Term Annotated Significant Expected Rank in classic classic      KS  elim weight
1  GO:0016020                            membrane      1079          13     8.37              1   0.025   0.327 0.025  0.031

> ##########  Biological process  #############

       GO.ID                                   Term Annotated Significant Expected Rank in classic classic   KS    elim weight
1  GO:0006810                              transport       940          14     5.88              1 0.00065 0.99 0.00065  0.408
2  GO:0008272                       sulfate transport         2           1     0.01              4 0.01247 0.96 0.01247  0.012
3  GO:0006750     glutathione biosynthetic process         4           1     0.03              5 0.02479 0.74 0.02479  0.025
4  GO:0006749        glutathione metabolic process         5           1     0.03              6 0.03089 0.91 0.03089  1.000
5  GO:0006813              potassium ion transport         8           1     0.05              7 0.04898 1.00 0.04898  0.049

##############################################
##                                          ##
##              Group Q                     ##
##                                          ##
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> ##########  Metabolic function  #############

       GO.ID                                   Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0008270                       zinc ion binding       649          64    44.92              1  0.0017   0.011 0.0017 0.0017
2  GO:0004198                       calpain activity         2           2     0.14              2  0.0048   0.999 0.0048 0.0048
3  GO:0003939          L-iditol 2-dehydrogenase activity        12           4     0.83              5  0.0072   0.912 0.0072 0.0072
4  GO:0016788 hydrolase activity, acting on ester bond...       281          30    19.45              8  0.0107   0.287 0.0107 0.6214
5  GO:0016564          transcriptional repressor activity         3           2     0.21              9  0.0137   0.992 0.0137 0.0137
6  GO:0003677                       DNA binding       664          59    45.96             12  0.0232   0.076 0.0232 0.0301
7  GO:0004089             carbonate dehydratase activity         4           2     0.28             13  0.0261   0.958 0.0261 0.0261
8  GO:0004300               enoyl-CoA hydratase activity         5           2     0.35             14  0.0415   0.964 0.0415 0.0415
9  GO:0008807 carboxyvinyl-carboxyphosphonate phosphor...         5           2     0.35             15  0.0415   0.719 0.0415 0.0415
10 GO:0016631 enoyl-[acyl-carrier-protein] reductase a...         5           2     0.35             16  0.0415   0.619 0.0415 0.0415
11 GO:0018498 2,3-dihydroxy-2,3-dihydro-phenylpropiona...         5           2     0.35             17  0.0415   0.619 0.0415 0.0415
12 GO:0018499 cis-2,3-dihydrodiol DDT dehydrogenase ac...         5           2     0.35             18  0.0415   0.619 0.0415 0.0415
13 GO:0018500 trans-9R,10R-dihydrodiolphenanthrene deh...         5           2     0.35             19  0.0415   0.619 0.0415 0.0415
14 GO:0018501 cis-chlorobenzene dihydrodiol dehydrogen...         5           2     0.35             20  0.0415   0.619 0.0415 0.0415
15 GO:0018502 2,5-dichloro-2,5-cyclohexadiene-1,4-diol...         5           2     0.35             21  0.0415   0.619 0.0415 0.0415
16 GO:0018503 trans-1,2-dihydrodiolphenanthrene dehydr...         5           2     0.35             22  0.0415   0.619 0.0415 0.0415
17 GO:0046556        alpha-N-arabinofuranosidase activity         5           2     0.35             23  0.0415   0.999 0.0415 0.0415
18 GO:0042578         phosphoric ester hydrolase activity        89          11     6.16             24  0.0421   0.897 0.0421 0.9032
19 GO:0031072                  heat shock protein binding        29           5     2.01             25  0.0464   0.977 0.0464 0.0464

> ##########  Cellular component  #############

       GO.ID                                   Term Annotated Significant Expected Rank in classic classic      KS   elim weight
1  GO:0005624                     membrane fraction         5           3     0.32              1  0.0023 0.98568 0.0023  0.063
2  GO:0043231     intracellular membrane-bound organelle       824          68    52.21              3  0.0036 0.00026 0.0036  0.179
3  GO:0005792                              microsome         4           2     0.25              5  0.0220 0.98854 0.0220  0.022
4  GO:0042598                     vesicular fraction         4           2     0.25              6  0.0220 0.98854 0.0220  1.000
5  GO:0000151                ubiquitin ligase complex        57           8     3.61              7  0.0250 0.70317 0.0250  0.025
6  GO:0005773                               vacuole         5           2     0.32             10  0.0351 0.98436 0.0351  1.000
7  GO:0005634                               nucleus       695          54    44.04             11  0.0409 2.1e-05 0.0409  0.393
```

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> ##########  Biological process  #############

        GO.ID                                     Term Annotated Significant Expected Rank in classic classic     KS   elim weight
1  GO:0050789            regulation of biological process       456          45    31.46               2  0.0075 0.1702 0.0075  0.632
2  GO:0006350                              transcription       517          49    35.67               3  0.0113 0.0086 0.0113  0.118
3  GO:0019222             regulation of metabolic process       418          41    28.84               4  0.0117 0.2904 0.0117  0.521
4  GO:0015976                          carbon utilization         3           2     0.21               5  0.0136 0.9999 0.0136  0.014
5  GO:0019219 regulation of nucleobase, nucleoside, nu...       410          39    28.29               6  0.0219 0.2262 0.0219  0.503
6  GO:0050794              regulation of cellular process       437          41    30.15               7  0.0234 0.1875 0.0234  0.794
7  GO:0031323    regulation of cellular metabolic process       413          39    28.50               8  0.0244 0.2492 0.0244  1.000
8  GO:0006355 regulation of transcription, DNA-depende...       395          37    27.25               9  0.0313 0.2354 0.0313  0.031
9  GO:0006564               L-serine biosynthetic process        18           4     1.24              10  0.0315 0.2653 0.0315  0.031
10 GO:0045449                 regulation of transcription       408          38    28.15              11  0.0316 0.2115 0.0316  0.712
11 GO:0016567                      protein ubiquitination        55           8     3.79              12  0.0333 0.9851 0.0333  0.033
12 GO:0032446 protein modification by small protein co...        55           8     3.79              13  0.0333 0.9851 0.0333  1.000
13 GO:0019566                 arabinose metabolic process         5           2     0.34              14  0.0413 0.9988 0.0413  1.000
14 GO:0046373               L-arabinose metabolic process         5           2     0.34              15  0.0413 0.9988 0.0413  0.041
15 GO:0006351                transcription, DNA-dependent       406          37    28.01              16  0.0448 0.1764 0.0448  1.000
16 GO:0032774                    RNA biosynthetic process       408          37    28.15              17  0.0477 0.1922 0.0477  0.745
```

Appendix G

Supplementaries for chapter 9

G.1 Schematic representations of polysaccharide structures

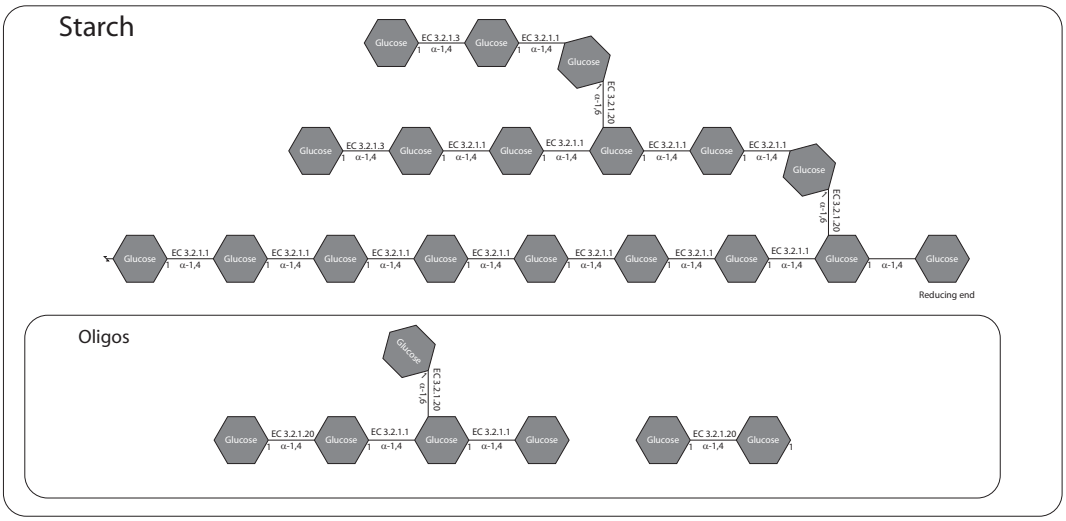

Figure G.1: Schematic representation of starch. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on Dumitriu (2005).

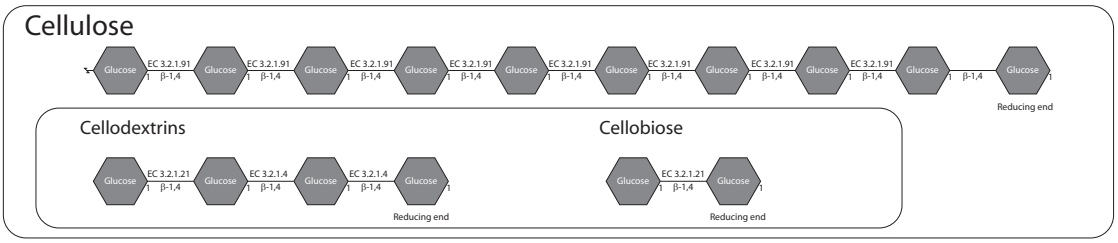

Figure G.2: Schematic representation of cellulose. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on de Vries and Visser (2001), Persson et al. (1991).

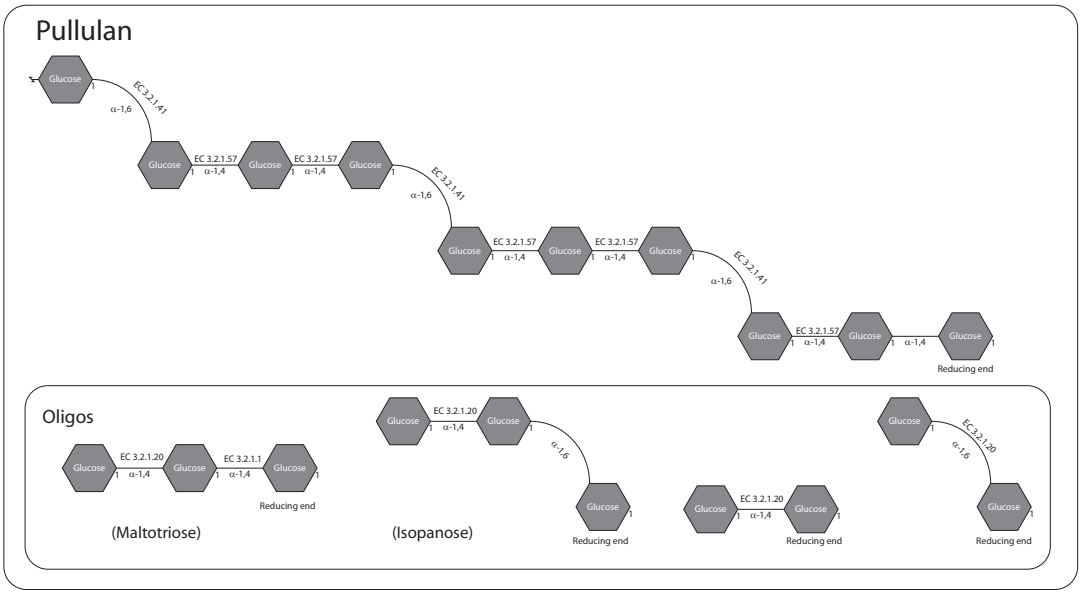

Figure G.3: Schematic representation of pullulan. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on Doman-Pytka and Bardowski (2004), Dumitriu (2005).

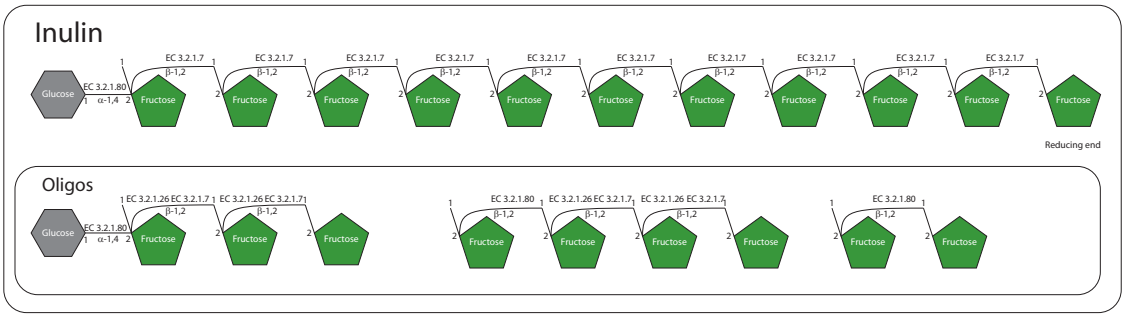

Figure G.4: Schematic representation of inulin. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on Niness (1999).

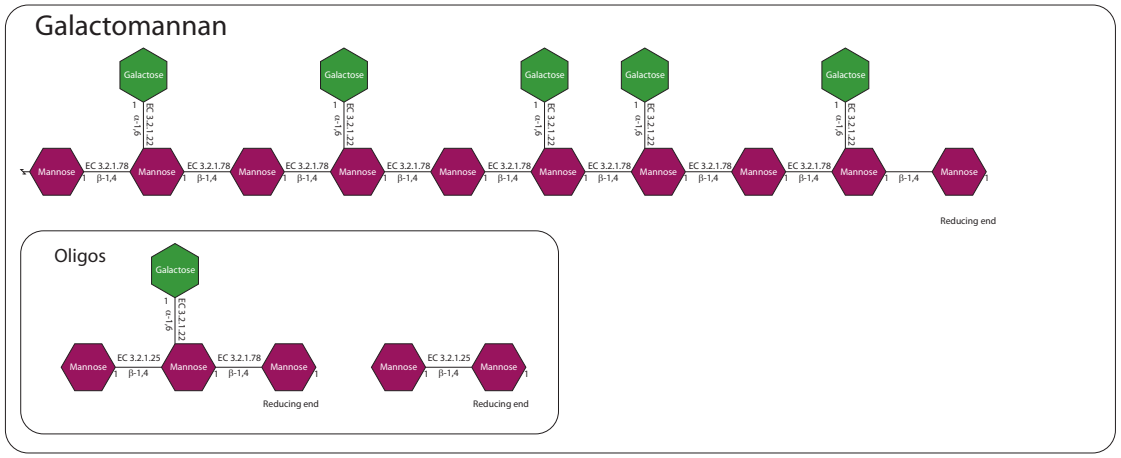

Figure G.5: Schematic representation of galactomannan. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on Daas et al. (2000), de Vries and Visser (2001) .

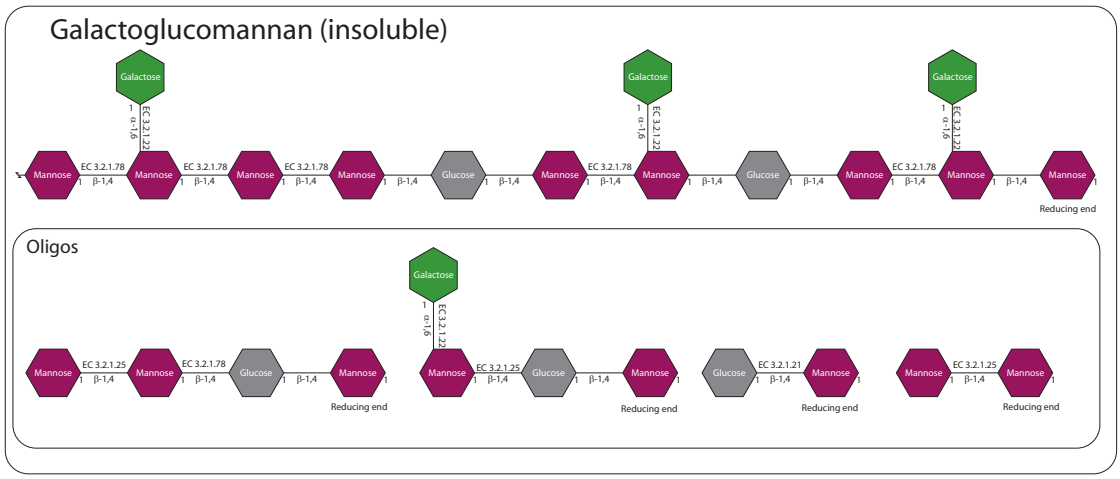

Figure G.6: Schematic representation of insoluble galactoglucomannan. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on de Vries and Visser (2001).

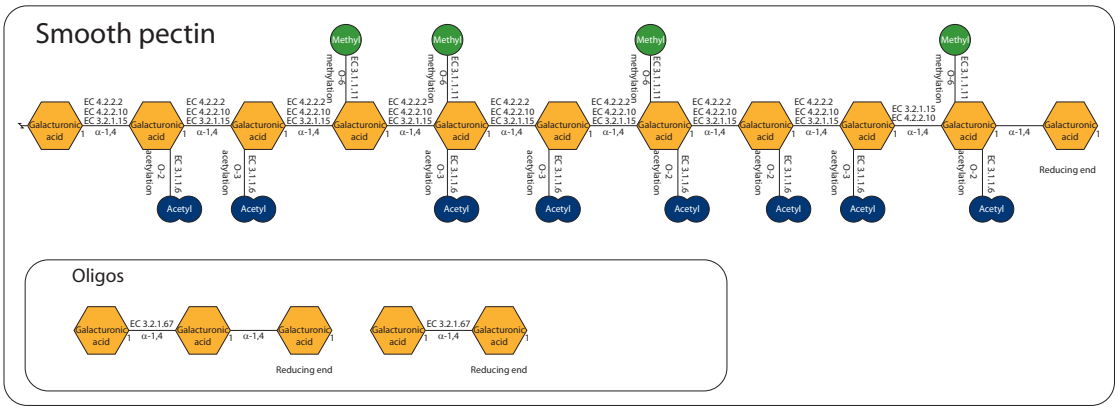

Figure G.7: Schematic representation of smooth pectin. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on de Vries and Visser (2001), Dumitriu (2005).

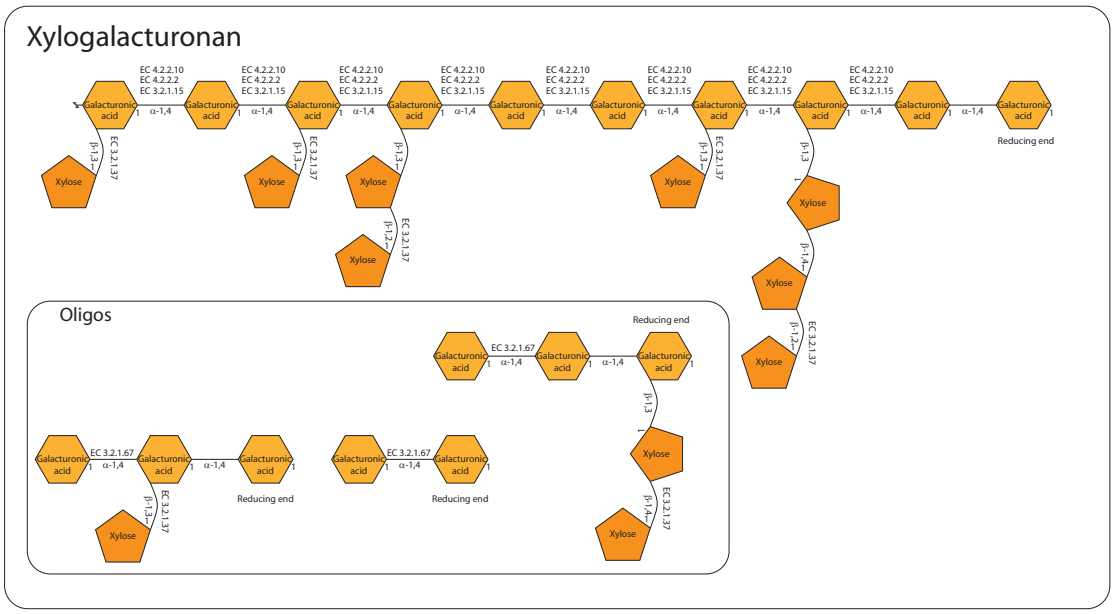

Figure G.8: Schematic representation of xylogalactouronan. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on de Vries and Visser (2001), le Goff et al. (2001), Nakamura et al. (2002), Zandleven et al. (2005, 2007).

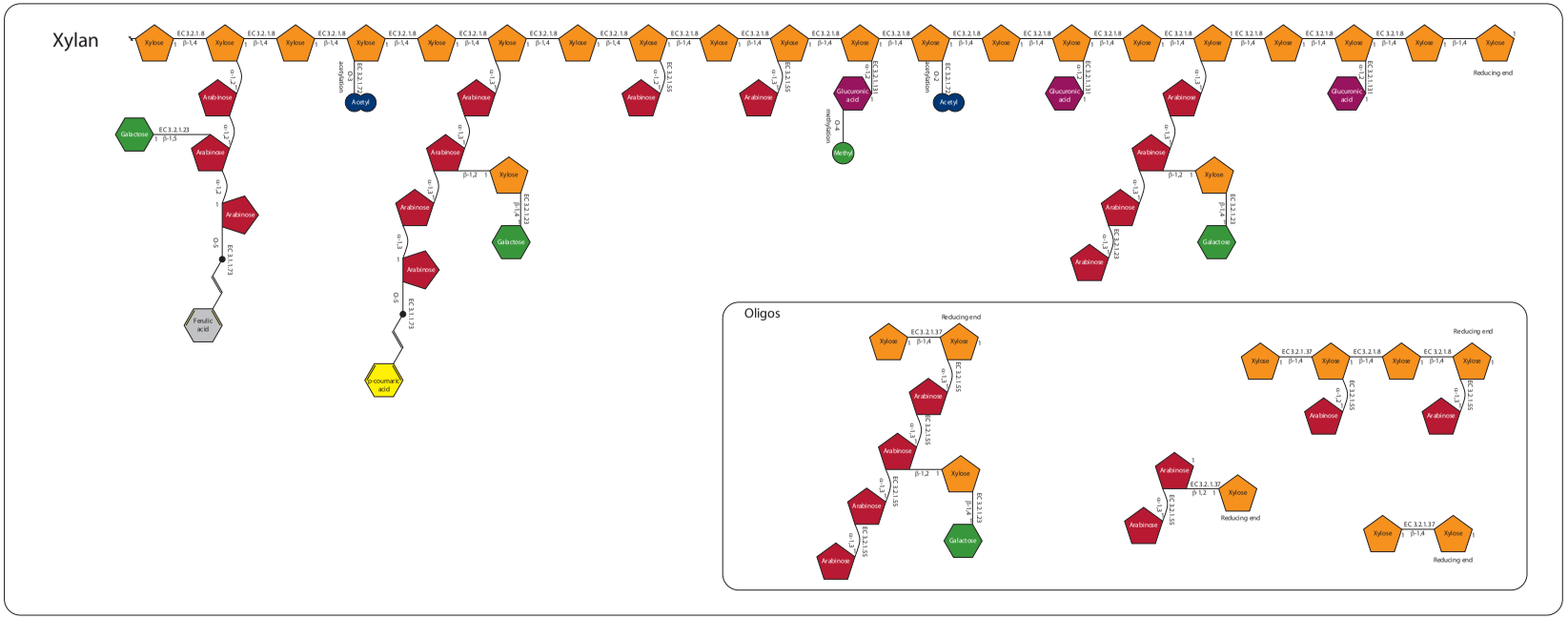

Figure G.9: Schematic representation of xylan. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on de Vries and Visser (2001), Biely (2003), Eriksson et al. (1990), Dumitriu (2005).

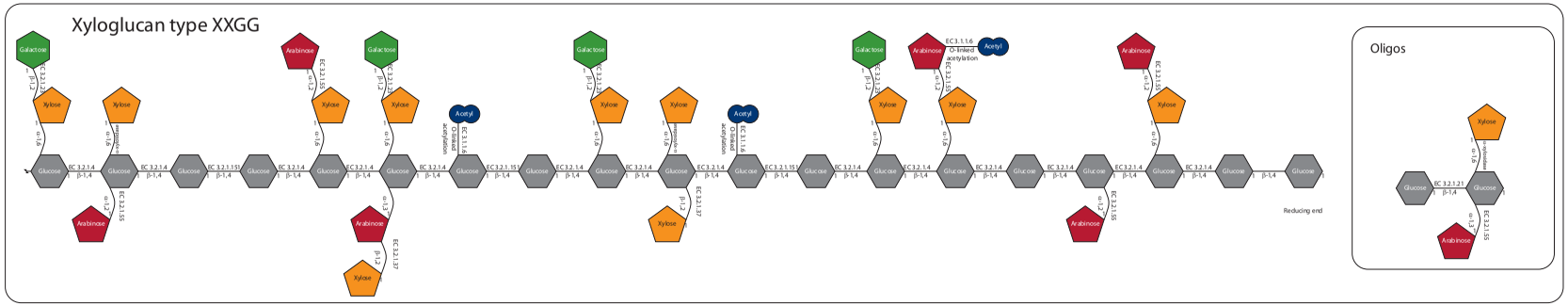

Figure G.10: Schematic representation of xyloglucan type XXGG. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on York et al. (1993), Vincken et al. (1997), de Vries and Visser (2001).

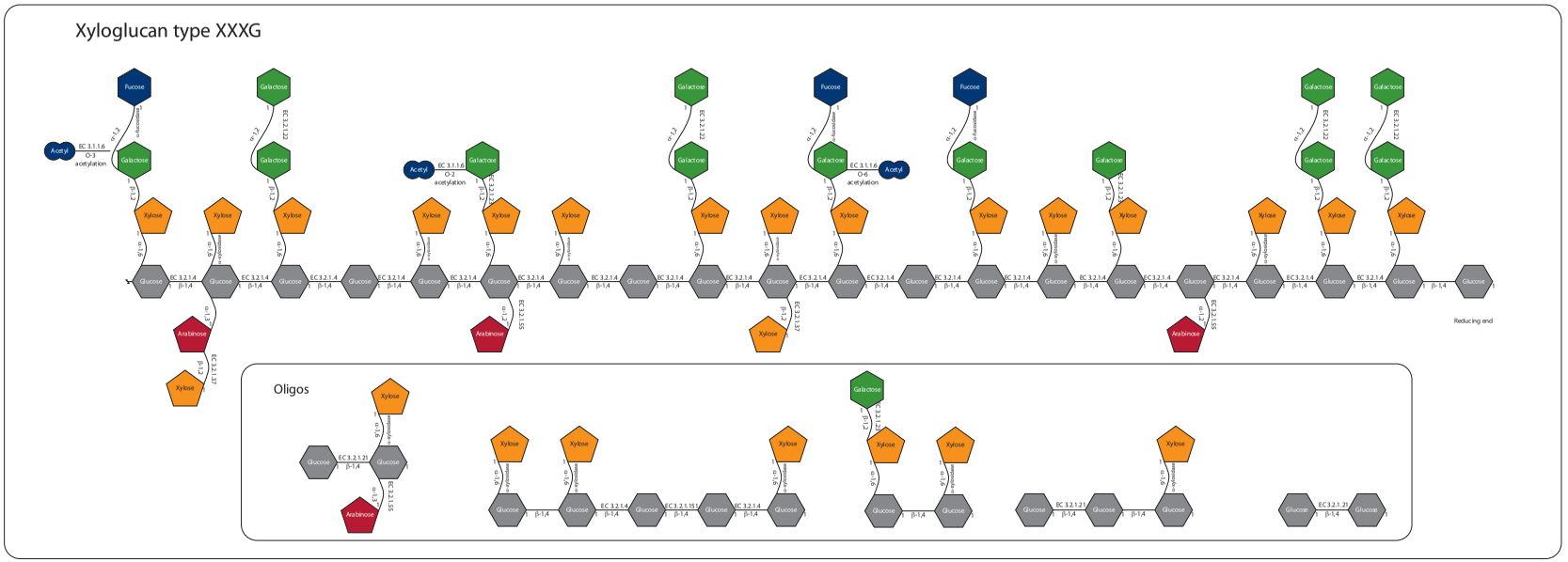

Figure G.11: Schematic representation of xyloglucan type XXXG. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on York et al. (1993), Vincken et al. (1997), de Vries and Visser (2001).

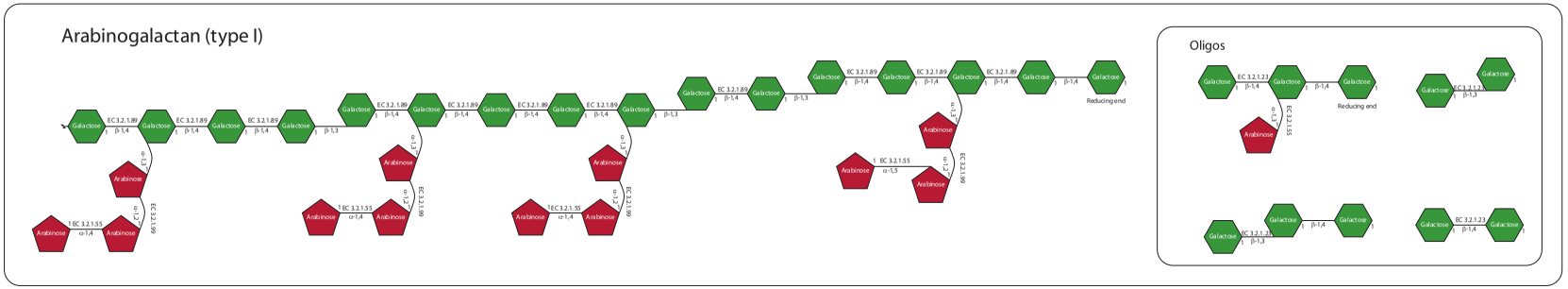

Figure G.12: Schematic representation of arabinogalactan type I. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on Hinz et al. (2005), de Vries et al. (2002a), Tischer et al. (2002).

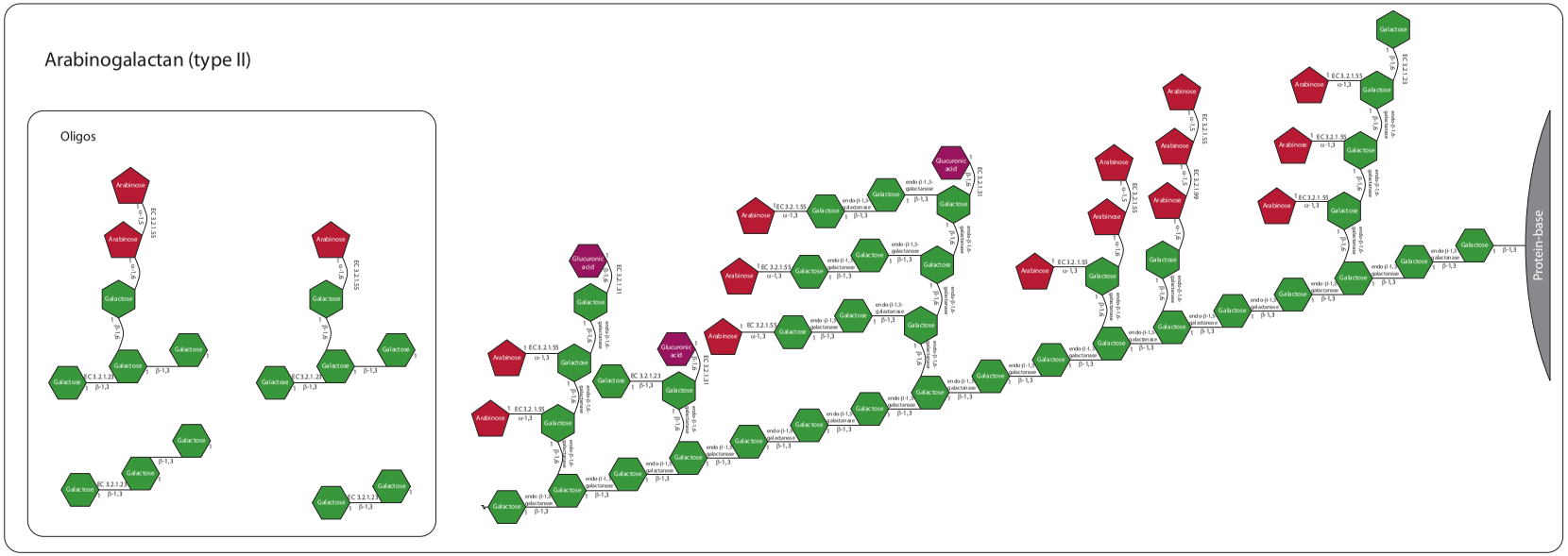

Figure G.13: Schematic representation of arabinogalactan type II (protein bound arabinogalactan). The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on Redgwell et al. (2002), Hinz et al. (2005), Haque et al. (2005), de Vries et al. (2002a).

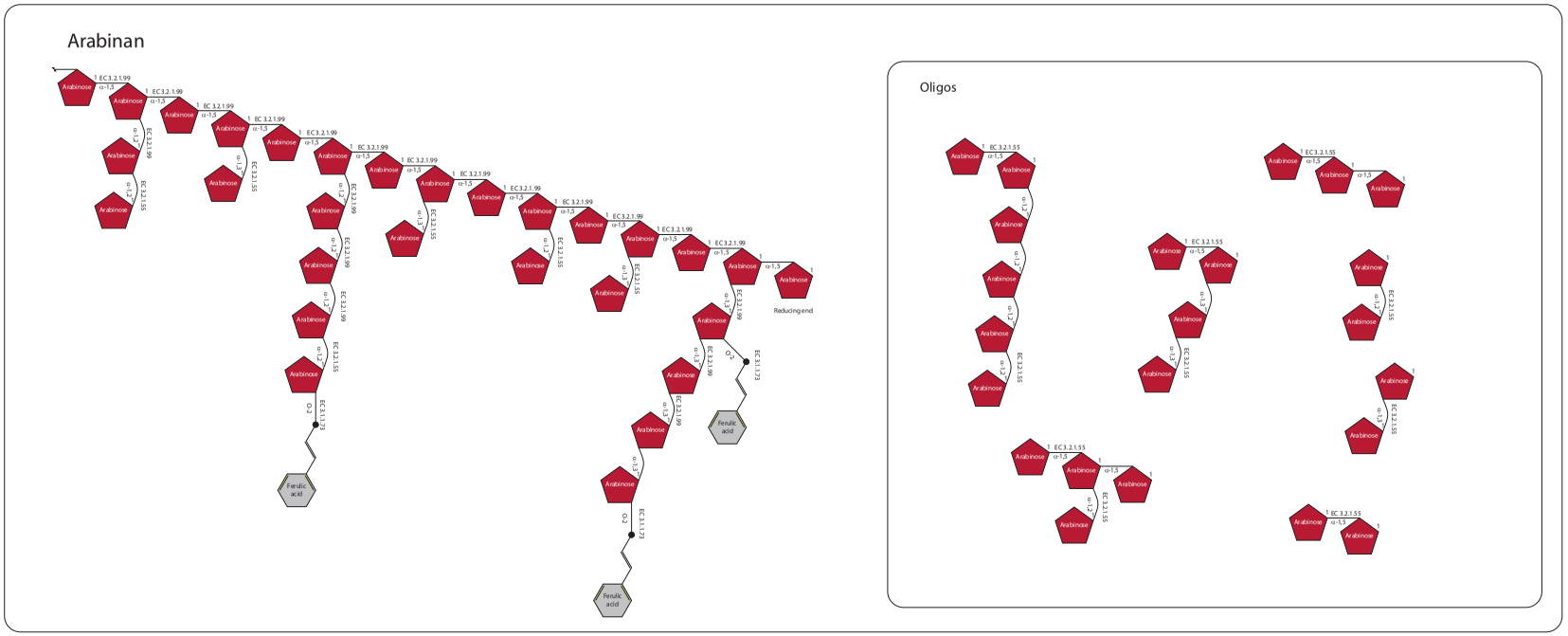

Figure G.14: Schematic representation of arabinan. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on Martinelli and Kinghorn (1994), Rombouts et al. (1988), Beldman et al. (1993).

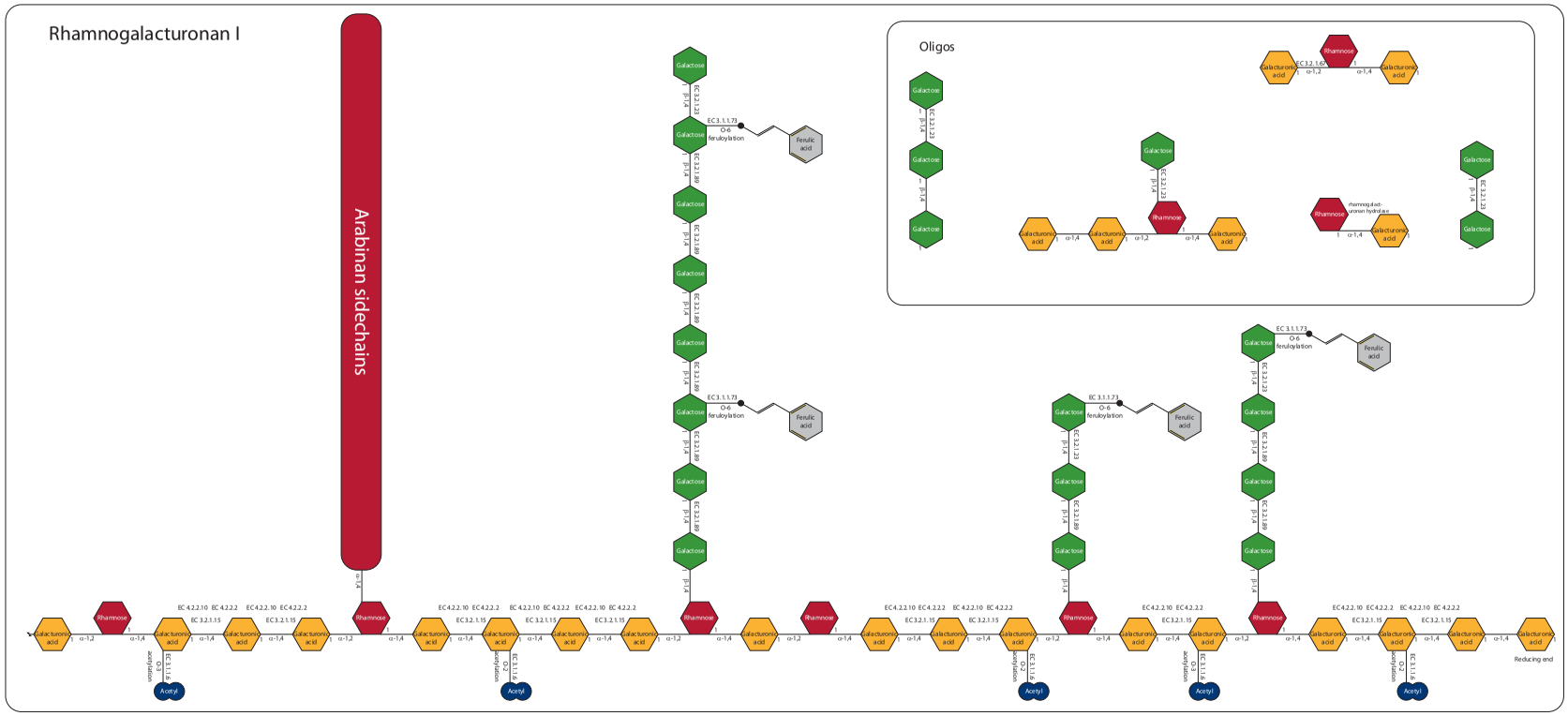

Figure G.15: Schematic representation of rhamnogalacturonan type I. The nature of the bonds between the sugar units are noted where they are known. The number of sides on the sugar polygons reflect the number of carbons of the sugar. The first carbon is indicated on all sugars with a 1 to clarify the bond configurations. Carbons are numbered clockwise from the first carbon with the two last carbons of the sugar (hexose or pentose) on the same corner of the polygon. The oligos are hypothetical hydrolysis products and sugars that appear due to the action of exo-acting enzymes. The structure is based on An et al. (1994), Renard et al. (1997), de Vries and Visser (2001).

G.2 Tables of bibliomic and sequence database survey results of polysaccharide degradation

Table G.1: Enzymatic activities required for the degradation of starch by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. Genes for *amyA* and *amyB* are not noted in the ATCC sequence list, as three almost identical genes exist *amyA*, *amyB* and ORF 140567. As the genes in the ATCC 1015 sequence are found by bi-directional best hits, it is, due to sequence differences between the two strains, not possible to determine 1:1 relationships for all three genes. However, ORF 140567 can be used as indicative for all of them. The list of necessary enzymes is gathered from Dumitriu (2005).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)					An02g00850	206445
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)					An02g06950	37060
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)	Boel et al. (1984b,a), Svensson et al. (1986)		*glaA*	P69328	An03g06550	213597
3.2.1.1	α-amylase					An04g06930	45304
3.2.1.1	α-amylase	Korman et al. (1990)		*amyA/amyB*	P56271	An05g02100	N/A
3.2.1.1	α-amylase					An09g03100	188489
3.2.1.1	α-amylase	Korman et al. (1990)		*amyA/amyB*	P56271	An12g06930	N/A
3.2.1.1	α-amylase					An09g03110	122069
3.2.1.1	α-amylase					An11g03340	140567
3.2.1.1	α-amylase					An12g02460	57002
3.2.1.1	α-amylase					An15g07800	182162
3.2.1.41	α-1,4-pullulanase	Sakano et al. (1972), Kobayashi and Sakano (1973)					
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)	Amirul et al. (1996)				An02g00850	206445
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)					An02g06950	37060
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)	Boel et al. (1984b,a), Svensson et al. (1986), Amirul et al. (1996)		*glaA*	P69328	An03g06550	213597
3.2.1.20	α-glucosidase					An13g03710	50927
3.2.1.20	α-glucosidase					An01g04880	55419
3.2.1.20	α-glucosidase	Nakamura et al. (1997)		*aglA/aglU*	P56526	An04g06920	214233
3.2.1.20	α-glucosidase					An07g00350	40261
3.2.1.20	α-glucosidase					An09g05880	128654
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)					An02g00850	206445
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)					An02g06950	37060
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)	Boel et al. (1984b,a), Svensson et al. (1986)		*glaA*	P69328	An03g06550	213597

Table G.2: Enzymatic activities required for the degradation of cellulose by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by de Vries and Visser (2001), Persson et al. (1991).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.91	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase)	Gielkens et al. (1999)		*cbhA*	Q9UVS9	An07g09330	53159
3.2.1.91	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase)	Gielkens et al. (1999)		*cbhB*	Q9UVS8	An01g11660	51773
3.2.1.91	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase)					An12g02220	54490
3.2.1.4	endo-glucanase	Hurst et al. (1977, 1978), van Peij et al. (1998a), Khademi et al. (2002)	Hasper et al. (2002)	*eglA*	O74705	An14g02760	211053
3.2.1.4	endo-glucanase	Akiba et al. (1995), van Peij et al. (1998a), Hong et al. (2001), Khademi et al. (2002)	Hasper et al. (2002)	*eglB*	O74706	An07g08950	209376
3.2.1.4	endo-glucanase					An03g01050	194447
3.2.1.4	endo-glucanase					An03g05380	N/A
3.2.1.4	endo-glucanase					An03g05530	191511
3.2.1.4	endo-glucanase					An04g08550	194765
3.2.1.4	endo-glucanase					An08g01760	133986
3.2.1.4	endo-glucanase					An15g04900	182430
3.2.1.21	β-glucosidase					An03g03740	213437
3.2.1.21	β-glucosidase					An03g05330	44520
3.2.1.21	β-glucosidase					An04g03170	131747
3.2.1.21	β-glucosidase					An06g02040	176601
3.2.1.21	β-glucosidase					An07g07630	139037
3.2.1.21	β-glucosidase					An07g09760	N/A
3.2.1.21	β-glucosidase					An08g08240	38077
3.2.1.21	β-glucosidase					An11g06080	208871
3.2.1.21	β-glucosidase					An11g06090	N/A
3.2.1.21	β-glucosidase					An14g01770	210981
3.2.1.21	β-glucosidase					An15g01890	182309
3.2.1.21	β-glucosidase					An15g04800	181816
3.2.1.21	β-glucosidase					An17g00520	129891
3.2.1.21	β-glucosidase	Witte and Wartenberg (1989), Himmel et al. (1993), Yan et al. (1998), Dan et al. (2000), Ramirez-Coronel et al. (2003), Seidle et al. (2004), Seidle and Huber (2005), Seidle et al. (2005, 2006)		*bgl1*	A2RAL4	An18g03570	56782

Table G.3: Enzymatic activities required for the degradation of pullulan by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by Doman-Pytka and Bardowski (2004).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.57	isopullulanase	Sakano et al. (1972), Aoki et al. (1996, 1997), Akeboshi et al. (2004), Mizuno et al. (2008)	Sakano et al. (1972), Aoki et al. (1996)	*ipuA*	O00105	N/A	N/A
3.2.1.41	pullulanase	Kobayashi and Sakano (1973)	Aoki et al. (1997)				
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)					An02g00850	206445
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)					An02g06950	37060
3.2.1.3	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)	Boel et al. (1984b,a), Svensson et al. (1986)		*glaA*	P69328	An03g06550	213597

Table G.4: Enzymatic activities required for the degradation of inulin by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by Niness (1999).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.7	endo-inulinase	Ohta et al. (1998), Akimoto et al. (1999), Zhang et al. (2004), Yuan et al. (2006)		*inuA/inuB*	O74641	An11g03200	52928
3.2.1.80	exo-inulinase	Moriyama et al. (2003), Yuan et al. (2006)		*inuE/inuF/inu1*	Q0ZR33	An12g08280	56664
3.2.1.80	exo-inulinase	Moriyama et al. (2003), Yuan et al. (2006)		*inuE/inuF/inu1*	Q0ZR33	An12g08280	56664
3.2.1.26	invertase	Wallis et al. (1997), Yuan et al. (2006), Goosen et al. (2007)	Wallis et al. (1997)	*sucB/suc2*	Q0ZR36	An15g00320	N/A

Table G.5: Enzymatic activities required for the degradation of galactomannan by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by Daas et al. (2000), de Vries and Visser (2001).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.78	Endo-1,4-β-D-mannanase	Ademark et al. (1998), Hägglund et al. (2001)	Ademark et al. (1998), Hägglund et al. (2001)			An05g01320	50378
3.2.1.78	Endo-1,4-β-D-mannanase					An15g07760	40875
3.2.1.25	β-mannosidase					An01g06630	172587
3.2.1.25	β-mannosidase	Ademark et al. (1999, 2001a), Bouquelet et al. (1978), Hägglund et al. (2001)	Ademark et al. (1999, 2001a), Hägglund et al. (2001)	*mndA*	Q9UUZ3	An11g06540	138876
3.2.1.22	α-galactosidase	Ademark et al. (2001a), de Vries et al. (1999a)	Ademark et al. (2001a)	*aglC*	Q9UUZ4	An09g00260	212736
3.2.1.22	α-galactosidase				An01g01320	172232	
3.2.1.22	α-galactosidase	de Vries et al. (1999a), Manzanares et al. (1998)		*aglB*	Q9Y865	An02g11150	207264
3.2.1.22	α-galactosidase	den Herder et al. (1992), de Vries et al. (1999a), Wallis et al. (2001)		*aglA*	A2QL72	An06g00170	37736
3.2.1.22	α-galactosidase					An11g06330	39180
3.2.1.22	α-galactosidase					An14g01800	185285

Table G.6: Enzymatic activities required for the degradation of soluble galactoglucomannan by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by Sims et al. (1997), Schröder et al. (2001), de Vries and Visser (2001), Capek et al. (2002)
.

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.78	Endo-1,4-β-D-mannanase	Ademark et al. (1998)	Ademark et al. (1998)			An05g01320	50378
3.2.1.78	Endo-1,4-β-D-mannanase					An15g07760	40875
3.2.1.25	β-mannosidase					An01g06630	172587
3.2.1.25	β-mannosidase	Ademark et al. (1999, 2001a), Bouquelet et al. (1978)	Ademark et al. (1999, 2001a)	*mndA*	Q9UUZ3	An11g06540	138876
3.2.1.22	α-galactosidase	Ademark et al. (2001a), de Vries et al. (1999a)	Ademark et al. (2001a)	*aglC*	Q9UUZ4	An09g00260	212736
3.2.1.22	α-galactosidase					An01g01320	172232
3.2.1.22	α-galactosidase	de Vries et al. (1999a), Manzanares et al. (1998)		*aglB*	Q9Y865	An02g11150	207264
3.2.1.22	α-galactosidase	den Herder et al. (1992), de Vries et al. (1999a), Wallis et al. (2001)		*aglA*	A2QL72	An06g00170	37736
3.2.1.22	α-galactosidase					An11g06330	39180
3.2.1.22	α-galactosidase					An14g01800	185285
3.2.1.21	β-glucosidase					An03g03740	213437
3.2.1.21	β-glucosidase					An03g05330	44520
3.2.1.21	β-glucosidase					An04g03170	131747
3.2.1.21	β-glucosidase					An06g02040	176601
3.2.1.21	β-glucosidase					An07g07630	139037
3.2.1.21	β-glucosidase					An07g09760	N/A
3.2.1.21	β-glucosidase					An08g08240	38077
3.2.1.21	β-glucosidase					An11g06080	208871
3.2.1.21	β-glucosidase					An11g06090	N/A
3.2.1.21	β-glucosidase					An14g01770	210981
3.2.1.21	β-glucosidase					An15g01890	182309
3.2.1.21	β-glucosidase					An15g04800	181816
3.2.1.21	β-glucosidase					An17g00520	129891
3.2.1.21	β-glucosidase	Witte and Wartenberg (1989), Himmel et al. (1993), Dan et al. (2000), Ramirez-Coronel et al. (2003), Seidle et al. (2004), Seidle and Huber (2005), Seidle et al. (2005, 2006)		*bgl1*	A2RAL4	An18g03570	56782
3.2.1.23	β-galactosidase					An01g10350	46429
3.2.1.23	β-galactosidase					An06g00290	177434
3.2.1.23	β-galactosidase					An07g04420	180727
3.2.1.23	β-galactosidase					An14g05820	41910
3.2.1.23	β-galactosidase	Kumar et al. (1992), de Vries et al. (1999a)		*lacA*	P29853	An01g12150	51764
3.1.1.6	Acetyl esterase					An02g02540	N/A

Table G.7: Enzymatic activities required for the degradation of insoluble galactoglucomannan by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by de Vries and Visser (2001).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.78	Endo-1,4-β-D-mannanase	Ademark et al. (1998)	Ademark et al. (1998)			An05g01320	50378
3.2.1.78	Endo-1,4-β-D-mannanase					An15g07760	40875
3.2.1.25	β-mannosidase					An01g06630	172587
3.2.1.25	β-mannosidase	Ademark et al. (1999, 2001a), Bouquelet et al. (1978)	Ademark et al. (1999, 2001a)	*mndA*	Q9UUZ3	An11g06540	138876
3.2.1.22	α-galactosidase	Ademark et al. (2001a), de Vries et al. (1999a)	Ademark et al. (2001a)	*aglC*	Q9UUZ4	An09g00260	212736
3.2.1.22	α-galactosidase					An01g01320	172232
3.2.1.22	α-galactosidase	de Vries et al. (1999a), Manzanares et al. (1998)		*aglB*	Q9Y865	An02g11150	207264
3.2.1.22	α-galactosidase	den Herder et al. (1992), de Vries et al. (1999a), Wallis et al. (2001)		*aglA*	A2QL72	An06g00170	37736
3.2.1.22	α-galactosidase					An11g06330	39180
3.2.1.22	α-galactosidase					An14g01800	185285
3.2.1.21	β-glucosidase					An03g03740	213437
3.2.1.21	β-glucosidase					An03g05330	44520
3.2.1.21	β-glucosidase					An04g03170	131747
3.2.1.21	β-glucosidase					An06g02040	176601
3.2.1.21	β-glucosidase					An07g07630	139037
3.2.1.21	β-glucosidase					An07g09760	N/A
3.2.1.21	β-glucosidase					An08g08240	38077
3.2.1.21	β-glucosidase					An11g06080	208871
3.2.1.21	β-glucosidase					An11g06090	N/A
3.2.1.21	β-glucosidase					An14g01770	210981
3.2.1.21	β-glucosidase					An15g01890	182309
3.2.1.21	β-glucosidase					An15g04800	181816
3.2.1.21	β-glucosidase					An17g00520	129891
3.2.1.21	β-glucosidase	Witte and Wartenberg (1989), Himmel et al. (1993), Dan et al. (2000), Ramirez-Coronel et al. (2003), Seidle et al. (2004), Seidle and Huber (2005), Seidle et al. (2005, 2006)		*bgl1*	A2RAL4	An18g03570	56782

Table G.8: Enzymatic activities required for the degradation of smooth pectin by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. Gene names in parentheses are genes that have not been characterized with classical molecular biological techniques, but identified from their expression profiles and sequence information. The list of necessary enzymes is gathered from the work by de Vries and Visser (2001).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
4.2.2.2	pectate lyase A	Benen et al. (2000), de Vries et al. (2002)	Benen et al. (2000)	*plyA*	Q9C2Z0	An10g00870	45021
4.2.2.10	pectin lyase	Harmsen et al. (1990), Kusters-Van Someren et al. (1991), Jenkins et al. (1996), Mayans et al. (1997), de Vries et al. (2002), Sánchez-Torres et al. (2003)	van Alebeek et al. (2002)	*pelA*	Q01172	An14g04370	41815
4.2.2.10	pectin lyase					An15g07160	210387
4.2.2.10	pectin lyase	Gysler et al. (1990), Harmsen et al. (1990), de Vries et al. (2002)		*pelD*	P22864	An19g00270	55212
4.2.2.10	pectin lyase					An11g04030	208760
4.2.2.10	pectin lyase	Kusters-Van Someren et al. (1992), Vitali et al. (1998), de Vries et al. (2002)		*pelB*	Q00205	An03g00190	45821
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxA)*		An01g14650	172236
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxB)*		An03g02080	194461
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(pgxB)*		An03g06740	191158
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(pgxA)*		An11g04040	178172
3.2.1.67	exo-poly-D-galacturonase	de Vries et al. (2002), Martens-Uzunova et al. (2006)		*(pgaX)*		An12g07500	42184
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxC)*		An18g04810	42917
3.2.1.15	endo-Polygalacturonase	Bussink et al. (1991a), van Pouderoyen et al. (2003), de Vries et al. (2002)	Benen et al. (1999), Pages et al. (2001)	*pgaI*	P26213	An01g11520	141677
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (1998), de Vries et al. (2002)	Benen et al. (1999)	*pgaE*	O42809	An01g14670	46255
3.2.1.15	endo-Polygalacturonase	Yang et al. (1997), Parenicova et al. (2000a), de Vries et al. (2002)	Parenicova et al. (2000a)	*pgaB*	P26214	An02g04900	52219
3.2.1.15	endo-Polygalacturonase			*(pgxC)*		An02g12450	172944
3.2.1.15	endo-Polygalacturonase	Bussink et al. (1992), de Vries et al. (2002)	Benen et al. (1999)	*pgaC*	Q12554	An05g02440	43957
3.2.1.15	endo-Polygalacturonase			*(rhgC)*		An06g02070	123651
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (2000b), de Vries et al. (2002)	Parenicova et al. (2000b)	*pgaD*	Q9P4W2	An09g03260	50161
3.2.1.15	endo-Polygalacturonase					An09g05920	N/A
3.2.1.15	endo-Polygalacturonase	Suykerbuyk et al. (1997), de Vries et al. (2002)	Suykerbuyk et al. (1997)	*rhgA*	P87160	An12g00950	189722
3.2.1.15	endo-Polygalacturonase	Keon and Waksman (1990), Bussink et al. (1990), Ruttkowski et al. (1991), Bussink et al. (1991b, 1992), Schröter et al. (1994), van Santen et al. (1999), Pagès et al. (2000), de Vries et al. (2002)	Benen et al. (1999), Limberg et al. (2000a,b), Pages et al. (2001)	*pgaII*		An15g05370	182156
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (2000a), de Vries et al. (2002)	Parenicova et al. (2000a)	*pgaA*		An16g06990	214598
3.2.1.15	rhamnogalacturonase B	Suykerbuyk et al. (1997), de Vries et al. (2002)	Suykerbuyk et al. (1997)	*rhgB*	P87161	An14g04200	211163
3.1.1.11	pectin methylesterase	Markovic and Joernvall (1990), Khanh et al. (1991), de Vries et al. (2002)	Kester et al. (2000), Limberg et al. (2000a,b)	*pmeA*	A2QHB7	An03g06310	44585
3.1.1.11	pectin methylesterase					An04g09690	214857
3.1.1.6	Acetyl esterase					An02g02540	N/A

Table G.9: Enzymatic activities required for the degradation of xylan by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by de Vries and Visser (2001), Biely (2003), Eriksson et al. (1990), Dumitriu (2005) .

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.8	Endo-(1,4)-β-xylanase					An01g14600	171269
3.2.1.8	Endo-(1,4)-β-xylanase	van den Broeck et al. (1992), Krengel and Dijkstra (1996)		*xynA*	P55329	An03g00940	57436
3.2.1.8	Endo-(1,4)-β-xylanase					An11g03120	38924
3.2.1.8	Endo-(1,4)-β-xylanase	Hessing et al. (1994), Tahir et al. (2002)		*exlA*		An14g07390	N/A
3.2.1.8	Endo-(1,4)-β-xylanase					An15g04550	183088
3.2.1.8	Endo-(1,4)-β-xylanase	van Ooyen et al. (1994), Kinoshita et al. (1995), van Peij et al. (1998a), Krisana et al. (2005)	Krisana et al. (2005)	*xynB/xlnB/xylB*	P55330	An01g00780	52071
3.2.1.37	Xylan 1,4-β-xylosidase	Claeyssens et al. (1971), van Peij et al. (1997, 1998a)	van Peij et al. (1997)	*xlnD*	O00089	An01g09960	205670
3.2.1.37	Xylan 1,4-β-xylosidase					An02g00140	174379
3.2.1.37	Xylan 1,4-β-xylosidase					An08g01900	47677
3.2.1.55	α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993c, 1994), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Pitson et al. (1997)	*abfA*	P42254	An01g00330	206387
3.2.1.55	α-L-arabinofuranosidase	Gielkens et al. (1997), van Peij et al. (1998a)	Kormelink et al. (1993a)	*axhA*	P79019	An03g00960	55136
3.2.1.55	α-L-arabinofuranosidase					An08g01710	38549
3.2.1.55	α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993b), Crous et al. (1996), Ruijter et al. (1997), van Peij et al. (1998a), de Vries et al. (2002), de Groot et al. (2003)		*abfB*	P42255	An15g02300	200605
3.2.1.55	α-L-arabinofuranosidase					An09g00880	131891
3.2.1.131	α-glucuronidase	van Peij et al. (1998a), de Vries et al. (2002b)		*aguA*		An14g05800	56619
3.1.1.72	Acetylxylan esterase	van Peij et al. (1998a)		*axeA*	A2QZI3	An09g01010	43522
3.1.1.73	Ferulic acid esterase A	Faulds and Williamson (1993), de Vries et al. (1997), van Peij et al. (1998a), de Vries et al. (1999b), de Vries and Visser (1999), Aliwan et al. (1999), de Vries et al. (2002)	Faulds and Williamson (1993), Aliwan et al. (1999)	*faeA*	O42807	An09g00120	51662
3.1.1.73	Ferulic acid esterase B	Kroon and Williamson (1996), de Vries et al. (2002)		*faeB*	Q8WZI8	N/A	51478
3.1.1.6	Acetyl esterase	Altaner et al. (2003)				An02g02540	N/A
3.2.1.23	β-galactosidase					An01g10350	46429
3.2.1.23	β-galactosidase					An06g00290	177434
3.2.1.23	β-galactosidase					An07g04420	180727
3.2.1.23	β-galactosidase					An14g05820	41910
3.2.1.23	β-galactosidase	Kumar et al. (1992), de Vries et al. (1999a)		*lacA*	P29853	An01g12150	51764

Table G.10: Enzymatic activities required for the degradation of xyloglucan type XXGG by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by York et al. (1993), Vincken et al. (1997), de Vries and Visser (2001).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.-	α-Xylosidase I	Matsushita et al. (1985)				N/A	N/A

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EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.-	α-Xylosidase II	Matsushita et al. (1987)				N/A	N/A
3.2.1.23	β-galactosidase					An01g10350	46429
3.2.1.23	β-galactosidase					An06g00290	177434
3.2.1.23	β-galactosidase					An07g04420	180727
3.2.1.23	β-galactosidase					An14g05820	41910
3.2.1.23	β-galactosidase	Kumar et al. (1992), de Vries et al. (1999a)		*lacA*	P29853	An01g12150	51764
3.2.1.4	endo-glucanase					An03g01050	194447
3.2.1.4	endo-glucanase					An03g05380	N/A
3.2.1.4	endo-glucanase					An03g05530	191511
3.2.1.4	endo-glucanase					An04g08550	194765
3.2.1.4	endo-glucanase					An08g01760	133986
3.2.1.4	endo-glucanase					An15g04900	182430
3.2.1.4	endo-glucanase	Hurst et al. (1977, 1978), van Peij et al. (1998a), Khademi et al. (2002)	Hasper et al. (2002)	*eglA*	O74705	An14g02760	211053
3.2.1.4	endo-glucanase	Akiba et al. (1995), van Peij et al. (1998a), Hong et al. (2001), Khademi et al. (2002)	Hasper et al. (2002)	*eglB*	O74706	An07g08950	209376
3.2.1.4	endo-glucanase	Hasper et al. (2002)	Hasper et al. (2002)	*eglC*	Q8TFP1	An01g01870	206333
3.2.1.151	xyloglucan-specific endo-β-1,4-glucanase	Master et al. (2008)	Master et al. (2008)	*xeg12A*	A1XP58	An01g03340	52011
3.2.1.55	exo-α-L-arabinofuranosidase (arabinoxylan arabinofuranohydrolase)	vd Veen et al. (1991), Flipphi et al. (1993c, 1994), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Pitson et al. (1997)	*abfA*	P42254	An01g00330	206387
3.2.1.55	exo-α-L-arabinofuranosidase (arabinoxylan arabinofuranohydrolase)					An08g01710	38549
3.2.1.55	exo-α-L-arabinofuranosidase (arabinoxylan arabinofuranohydrolase)	vd Veen et al. (1991, 1993), Flipphi et al. (1993b), Crous et al. (1996), Ruijter et al. (1997), van Peij et al. (1998a), de Vries et al. (2002), de Groot et al. (2003)		*abfB*	P42255	An15g02300	200605
3.2.1.55	exo-α-L-arabinofuranosidase (arabinoxylan arabinofuranohydrolase)					An09g00880	131891
3.1.1.6	Acetyl esterase	Altaner et al. (2003)				An02g02540	N/A
3.2.1.37	Xylan 1,4-β-xylosidase	Claeyssens et al. (1971), van Peij et al. (1997, 1998a)		*xlnD*	O00089	An01g09960	205670
3.2.1.37	Xylan 1,4-β-xylosidase					An02g00140	174379
3.2.1.37	Xylan 1,4-β-xylosidase					An08g01900	47677
3.2.1.21	β-glucosidase					An03g03740	213437
3.2.1.21	β-glucosidase					An03g05330	44520
3.2.1.21	β-glucosidase					An04g03170	131747
3.2.1.21	β-glucosidase					An06g02040	176601
3.2.1.21	β-glucosidase					An07g07630	139037
3.2.1.21	β-glucosidase					An07g09760	N/A
3.2.1.21	β-glucosidase					An08g08240	38077
3.2.1.21	β-glucosidase					An11g06080	208871
3.2.1.21	β-glucosidase					An11g06090	N/A
3.2.1.21	β-glucosidase					An14g01770	210981
3.2.1.21	β-glucosidase					An15g01890	182309
3.2.1.21	β-glucosidase					An15g04800	181816
3.2.1.21	β-glucosidase					An17g00520	129891

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EC number	Name	Gene characterization	Details on the specificity	Gene	Uniprot	CBS 513.88	ATCC 1015
3.2.1.21	β-glucosidase	Witte and Wartenberg (1989), Himmel et al. (1993), Yan et al. (1998), Dan et al. (2000), Ramirez-Coronel et al. (2003), Seidle et al. (2004), Seidle and Huber (2005), Seidle et al. (2005, 2006)		*bgl1*	A2RAL4	An18g03570	56782

Table G.11: Enzymatic activities required for the degradation of xyloglucan type XXXG by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by York et al. (1993), Vincken et al. (1997), de Vries and Visser (2001).

EC number	Name	Gene characterization	Details on the specificity	Gene	Uniprot	CBS 513.88	ATCC 1015
3.2.1.-	α-Xylosidase I	Matsushita et al. (1985)				N/A	N/A
3.2.1.-	α-Xylosidase II	Matsushita et al. (1987)				N/A	N/A
3.2.1.23	β-galactosidase					An01g10350	46429
3.2.1.23	β-galactosidase					An06g00290	177434
3.2.1.23	β-galactosidase					An07g04420	180727
3.2.1.23	β-galactosidase					An14g05820	41910
3.2.1.23	β-galactosidase	Kumar et al. (1992), de Vries et al. (1999a)		*lacA*	P29853	An01g12150	51764
3.2.1.4	endo-glucanase					An03g01050	194447
3.2.1.4	endo-glucanase					An03g05380	N/A
3.2.1.4	endo-glucanase					An03g05530	191511
3.2.1.4	endo-glucanase					An04g08550	194765
3.2.1.4	endo-glucanase					An08g01760	133986
3.2.1.4	endo-glucanase					An15g04900	182430
3.2.1.4	endo-glucanase	Hurst et al. (1977, 1978), van Peij et al. (1998a), Khademi et al. (2002)	Hasper et al. (2002)	*eglA*	O74705	An14g02760	211053
3.2.1.4	endo-glucanase	Akiba et al. (1995), van Peij et al. (1998a), Hong et al. (2001), Khademi et al. (2002)	Hasper et al. (2002)	*eglB*	O74706	An07g08950	209376
3.2.1.4	endo-glucanase	Hasper et al. (2002)	Hasper et al. (2002)	*eglC*	Q8TFP1	An01g01870	206333
3.2.1.151	xyloglucan-specific endo-β-1,4-glucanase	Master et al. (2008)	Master et al. (2008)	*xeg12A*	A1XP58	An01g03340	52011
	1,2-α-L-fucosidase	Bahl (1970)	Bahl (1970)	*fucA*			
3.2.1.55	exo-α-L-arabinofuranosidase (arabinoxylan arabinofuranohydrolase)	vd Veen et al. (1991), Flipphi et al. (1993c, 1994), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Pitson et al. (1997)	*abfA*	P42254	An01g00330	206387
3.2.1.55	exo-α-L-arabinofuranosidase (arabinoxylan arabinofuranohydrolase)					An08g01710	38549
3.2.1.55	exo-α-L-arabinofuranosidase (arabinoxylan arabinofuranohydrolase)	vd Veen et al. (1991, 1993), Flipphi et al. (1993b), Crous et al. (1996), Ruijter et al. (1997), van Peij et al. (1998a), de Vries et al. (2002), de Groot et al. (2003)		*abfB*	P42255	An15g02300	200605
3.2.1.55	exo-α-L-arabinofuranosidase (arabinoxylan arabinofuranohydrolase)					An09g00880	131891
3.1.1.6	Acetyl esterase	Altaner et al. (2003)				An02g02540	N/A
3.2.1.37	Xylan 1,4-β-xylosidase	Claeyssens et al. (1971), van Peij et al. (1997, 1998a)		*xlnD*	O00089	An01g09960	205670
3.2.1.37	Xylan 1,4-β-xylosidase					An02g00140	174379
3.2.1.37	Xylan 1,4-β-xylosidase					An08g01900	47677

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EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.21	β-glucosidase					An03g03740	213437
3.2.1.21	β-glucosidase					An03g05330	44520
3.2.1.21	β-glucosidase					An04g03170	131747
3.2.1.21	β-glucosidase					An06g02040	176601
3.2.1.21	β-glucosidase					An07g07630	139037
3.2.1.21	β-glucosidase					An07g09760	N/A
3.2.1.21	β-glucosidase					An08g08240	38077
3.2.1.21	β-glucosidase					An11g06080	208871
3.2.1.21	β-glucosidase					An11g06090	N/A
3.2.1.21	β-glucosidase					An14g01770	210981
3.2.1.21	β-glucosidase					An15g01890	182309
3.2.1.21	β-glucosidase					An15g04800	181816
3.2.1.21	β-glucosidase					An17g00520	129891
3.2.1.21	β-glucosidase	Witte and Wartenberg (1989), Himmel et al. (1993), Yan et al. (1998), Dan et al. (2000), Ramirez-Coronel et al. (2003), Seidle et al. (2004), Seidle and Huber (2005), Seidle et al. (2005, 2006)		*bgl1*	A2RAL4	An18g03570	56782
3.2.1.22	α-galactosidase	Ademark et al. (2001a), de Vries et al. (1999a)	Ademark et al. (2001a)	*aglC*	Q9UUZ4	An09g00260	212736
3.2.1.22	α-galactosidase					An01g01320	172232
3.2.1.22	α-galactosidase	de Vries et al. (1999a), Manzanares et al. (1998)		*aglB*	Q9Y865	An02g11150	207264
3.2.1.22	α-galactosidase	den Herder et al. (1992), de Vries et al. (1999a), Wallis et al. (2001)		*aglA*	A2QL72	An06g00170	37736
3.2.1.22	α-galactosidase					An11g06330	39180
3.2.1.22	α-galactosidase					An14g01800	185285

Table G.12: Enzymatic activities required for the degradation of xylogalacturonan by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. Gene names in parentheses are genes that have not been characterized with classical molecular biological techniques, but identified from their expression profiles and sequence information. The list of necessary enzymes is gathered from the work by de Vries and Visser (2001), le Goff et al. (2001), Nakamura et al. (2002), Zandleven et al. (2005, 2007) .

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
4.2.2.2	pectate lyase A	Benen et al. (2000), de Vries et al. (2002)	Benen et al. (2000)	*plyA*	Q9C2Z0	An10g00870	45021
4.2.2.10	pectin lyase	Harmsen et al. (1990), Kusters-Van Someren et al. (1991), Jenkins et al. (1996), Mayans et al. (1997), de Vries et al. (2002), Sánchez-Torres et al. (2003)	van Alebeek et al. (2002)	*pelA*	Q01172	An14g04370	41815
4.2.2.10	pectin lyase					An15g07160	210387
4.2.2.10	pectin lyase	Gysler et al. (1990), Harmsen et al. (1990), de Vries et al. (2002)		*pelD*	P22864	An19g00270	55212
4.2.2.10	pectin lyase					An11g04030	208760
4.2.2.10	pectin lyase	Kusters-Van Someren et al. (1992), Vitali et al. (1998), de Vries et al. (2002)		*pelB*	Q00205	An03g00190	45821
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxA)*		An01g14650	172236
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxB)*		An03g02080	194461
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(pgxB)*		An03g06740	191158
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(pgxA)*		An11g04040	178172
3.2.1.67	exo-poly-D-galacturonase	de Vries et al. (2002), Martens-Uzunova et al. (2006)		*(pgaX)*		An12g07500	42184
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxC)*		An18g04810	42917
3.2.1.15	endo-Polygalacturonase	Bussink et al. (1991a), van Pouderoyen et al. (2003), de Vries et al. (2002)	Benen et al. (1999), Pages et al. (2001)	*pgaI*	P26213	An01g11520	141677
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (1998), de Vries et al. (2002)	Benen et al. (1999)	*pgaE*	O42809	An01g14670	46255
3.2.1.15	endo-Polygalacturonase	Yang et al. (1997), Parenicova et al. (2000a), de Vries et al. (2002)	Parenicova et al. (2000a)	*pgaB*	P26214	An02g04900	52219
3.2.1.15	endo-Polygalacturonase			*(pgxC)*		An02g12450	172944
3.2.1.15	endo-Polygalacturonase	Bussink et al. (1992), de Vries et al. (2002)	Benen et al. (1999)	*pgaC*	Q12554	An05g02440	43957
3.2.1.15	endo-Polygalacturonase			*(rhgC)*		An06g02070	123651
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (2000b), de Vries et al. (2002)	Parenicova et al. (2000b)	*pgaD*	Q9P4W2	An09g03260	50161
3.2.1.15	endo-Polygalacturonase					An09g05920	N/A
3.2.1.15	endo-Polygalacturonase	Suykerbuyk et al. (1997), de Vries et al. (2002)	Suykerbuyk et al. (1997)	*rhgA*	P87160	An12g00950	189722
3.2.1.15	endo-Polygalacturonase	Keon and Waksman (1990), Bussink et al. (1990), Ruttkowski et al. (1991), Bussink et al. (1991b, 1992), Schröter et al. (1994), van Santen et al. (1999), Pagès et al. (2000), de Vries et al. (2002)	Benen et al. (1999), Limberg et al. (2000a,b), Pages et al. (2001)	*pgaII*		An15g05370	182156
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (2000a), de Vries et al. (2002)	Parenicova et al. (2000a)	*pgaA*		An16g06990	214598
3.2.1.15	rhamnogalacturonase B	Suykerbuyk et al. (1997), de Vries et al. (2002)	Suykerbuyk et al. (1997)	*rhgB*	P87161	An14g04200	211163
3.2.1.37	Xylan 1,4-β-xylosidase	Claeyssens et al. (1971), van Peij et al. (1997, 1998a)		*xlnD*	O00089	An01g09960	205670
3.2.1.37	Xylan 1,4-β-xylosidase					An02g00140	174379
3.2.1.37	Xylan 1,4-β-xylosidase					An08g01900	47677

Table G.13: Enzymatic activities required for the degradation of arabinogalactan I by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by Hinz et al. (2005), de Vries et al. (2002a), Tischer et al. (2002).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.89	β-1,4-endogalactanase					An16g06590	N/A
3.2.1.89	β-1,4-endogalactanase	Yamaguchi et al. (1995), de Vries et al. (2002a)	Yamaguchi et al. (1995), de Vries et al. (2002a)	*galA*	Q8X168	An18g05940	187227
3.2.1.23	β-galactosidase					An01g10350	46429
3.2.1.23	β-galactosidase					An06g00290	177434
3.2.1.23	β-galactosidase					An07g04420	180727
3.2.1.23	β-galactosidase					An14g05820	41910
3.2.1.23	β-galactosidase	Kumar et al. (1992), de Vries et al. (1999a)		*lacA*	P29853	An01g12150	51764
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993c, 1994), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Pitson et al. (1997)	*abfA*	P42254	An01g00330	206387
3.2.1.55	exo-α-L-arabinofuranosidase					An08g01710	38549
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993b), Crous et al. (1996), Ruijter et al. (1997), van Peij et al. (1998a), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Beldman et al. (1993), Schrøder et al. (1999)	*abfB*	P42255	An15g02300	200605
3.2.1.55	exo-α-L-arabinofuranosidase					An09g00880	131891
3.2.1.99	endo-1,5-α-L-arabinanase					An02g01400	134398
3.2.1.99	endo-1,5-α-L-arabinanase					An02g10550	197735
3.2.1.99	endo-1,5-α-L-arabinanase	vd Veen et al. (1991), Flipphi et al. (1993a), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)		*abnA*	P42256	An09g01190	203143
3.2.1.99	endo-1,5-α-L-arabinanase					An16g02730	184195

Table G.14: Enzymatic activities required for the degradation of arabinogalactan II by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by Redgwell et al. (2002), Hinz et al. (2005), Haque et al. (2005), de Vries et al. (2002a).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.31	β-glucuronidase					An01g01260	46827
3.2.1.31	β-glucuronidase					An05g02410	189620
	endo-β-1,3-galactanase					N/A	N/A
	endo-β-1,6-galactanase					N/A	N/A
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993c, 1994), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Pitson et al. (1997)	*abfA*	P42254	An01g00330	206387
3.2.1.55	exo-α-L-arabinofuranosidase					An08g01710	38549
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993b), Crous et al. (1996), Ruijter et al. (1997), van Peij et al. (1998a), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Beldman et al. (1993), Schrøder et al. (1999)	*abfB*	P42255	An15g02300	200605
3.2.1.55	exo-α-L-arabinofuranosidase					An09g00880	131891
3.2.1.99	endo-1,5-α-L-arabinanase					An02g01400	134398
3.2.1.99	endo-1,5-α-L-arabinanase					An02g10550	197735
3.2.1.99	endo-1,5-α-L-arabinanase	vd Veen et al. (1991), Flipphi et al. (1993a), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)		*abnA*	P42256	An09g01190	203143
3.2.1.99	endo 1,5-α-L-arabinanase					An16g02730	184195
3.2.1.23	β-galactosidase					An01g10350	46429
3.2.1.23	β-galactosidase					An06g00290	177434
3.2.1.23	β-galactosidase					An07g04420	180727
3.2.1.23	β-galactosidase					An14g05820	41910
3.2.1.23	β-galactosidase	Kumar et al. (1992), de Vries et al. (1999a)		*lacA*	P29853	An01g12150	51764

Table G.15: Enzymatic activities required for the degradation of arabinan by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. The list of necessary enzymes is gathered from the work by Martinelli and Kinghorn (1994), Beldman et al. (1993) .

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991), Flipphi et al. (1993c), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Pitson et al. (1997)	*abfA*	P42254	An01g00330	206387
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991), Flipphi et al. (1993c, 1994), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)				An08g01710	38549
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993b), Crous et al. (1996), Ruijter et al. (1997), van Peij et al. (1998a), de Vries et al. (2002), de Groot et al. (2003)		*abfB*	P42255	An15g02300	200605
3.2.1.55	exo-α-L-arabinofuranosidase					An09g00880	131891
3.2.1.99	endo-1,5-α-L-arabinanase					An02g01400	134398
3.2.1.99	endo-1,5-α-L-arabinanase					An02g10550	197735
3.2.1.99	endo-1,5-α-L-arabinanase	vd Veen et al. (1991), Flipphi et al. (1993a), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)		*abnA*	P42256	An09g01190	203143
3.2.1.99	endo-1,5-α-L-arabinanase					An16g02730	184195
none	exo-arabinase	de Vries and Visser (2001)					N/A
3.1.1.73	Ferulic acid esterase A	Faulds and Williamson (1993), de Vries et al. (1997), van Peij et al. (1998a), de Vries et al. (1999b), de Vries and Visser (1999), Aliwan et al. (1999), de Vries et al. (2002)	Faulds and Williamson (1993), Aliwan et al. (1999)	*faeA*	O42807	An09g00120	51662
3.1.1.73	Ferulic acid esterase B	Kroon and Williamson (1996), de Vries et al. (2002)		*faeB*	Q8WZI8	N/A	51478

Table G.16: Enzymatic activities required for the degradation of rhamnogalacturonan I by *A. niger*. For each isoenzyme, putative or characterized, is noted literature references and the gene ID in the sequencings of *A. niger* CBS 513.88 and ATCC 1015. Gene names in parentheses are genes that have not been characterized with classical molecular biological techniques, but identified from their expression profiles and sequence information. The list of necessary enzymes is gathered from the work by An et al. (1994), Renard et al. (1997), de Vries and Visser (2001).

EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
No EC	rhamnogalacturonan hydrolase	Suykerbuyk et al. (1997), de Vries et al. (2002)		*rglA*	Q8NJK5	An14g01130	210947
4.2.2.2	pectate lyase A	Benen et al. (2000), de Vries et al. (2002)	Benen et al. (2000)	*plyA*	Q9C2Z0	An10g00870	45021
4.2.2.10	pectin lyase	Harmsen et al. (1990), Kusters-Van Someren et al. (1991), Jenkins et al. (1996), Mayans et al. (1997), de Vries et al. (2002), Sánchez-Torres et al. (2003)	van Alebeek et al. (2002)	*pelA*	Q01172	An14g04370	41815
4.2.2.10	pectin lyase					An15g07160	210387
4.2.2.10	pectin lyase	Gysler et al. (1990), Harmsen et al. (1990), de Vries et al. (2002)		*pelD*	P22864	An19g00270	55212
4.2.2.10	pectin lyase					An11g04030	208760
4.2.2.10	pectin lyase	Kusters-Van Someren et al. (1992), Vitali et al. (1998), de Vries et al. (2002)		*pelB*	Q00205	An03g00190	45821

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EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxA)*		An01g14650	172236
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxB)*		An03g02080	194461
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(pgxB)*		An03g06740	191158
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(pgxA)*		An11g04040	178172
3.2.1.67	exo-poly-D-galacturonase	de Vries et al. (2002), Martens-Uzunova et al. (2006)		*(pgaX)*		An12g07500	42184
3.2.1.67	exo-poly-D-galacturonase	Martens-Uzunova et al. (2006)		*(rgxC)*		An18g04810	42917
3.2.1.15	endo-Polygalacturonase	Bussink et al. (1991a), van Pouderoyen et al. (2003), de Vries et al. (2002)	Benen et al. (1999), Pages et al. (2001)	*pgaI*	P26213	An01g11520	141677
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (1998), de Vries et al. (2002)	Benen et al. (1999)	*pgaE*	O42809	An01g14670	46255
3.2.1.15	endo-Polygalacturonase	Yang et al. (1997), Parenicova et al. (2000a), de Vries et al. (2002)	Parenicova et al. (2000a)	*pgaB*	P26214	An02g04900	52219
3.2.1.15	endo-Polygalacturonase			*(pgxC)*		An02g12450	172944
3.2.1.15	endo-Polygalacturonase	Bussink et al. (1992), de Vries et al. (2002)	Benen et al. (1999)	*pgaC*	Q12554	An05g02440	43957
3.2.1.15	endo-Polygalacturonase			*(rhgC)*		An06g02070	123651
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (2000b), de Vries et al. (2002)	Parenicova et al. (2000b)	*pgaD*	Q9P4W2	An09g03260	50161
3.2.1.15	endo-Polygalacturonase					An09g05920	N/A
3.2.1.15	endo-Polygalacturonase	Suykerbuyk et al. (1997), de Vries et al. (2002)	Suykerbuyk et al. (1997)	*rhgA*	P87160	An12g00950	189722
3.2.1.15	endo-Polygalacturonase	Keon and Waksman (1990), Bussink et al. (1990), Ruttkowski et al. (1991), Bussink et al. (1991b, 1992), Schröter et al. (1994), van Santen et al. (1999), Pagès et al. (2000), de Vries et al. (2002)	Benen et al. (1999), Limberg et al. (2000a,b), Pages et al. (2001)	*pgaII*		An15g05370	182156
3.2.1.15	endo-Polygalacturonase	Parenicova et al. (2000a), de Vries et al. (2002)	Parenicova et al. (2000a)	*pgaA*		An16g06990	214598
3.2.1.15	rhamnogalacturonase B	Suykerbuyk et al. (1997), de Vries et al. (2002)	Suykerbuyk et al. (1997)	*rhgB*	P87161	An14g04200	211163
No EC	rhamnogalacturonan acetylesterase (*rgaeA*)	de Vries et al. (2000), de Vries and Visser (2001), de Vries et al. (2002)		*rgaeA*	Q96VT8	An09g02160	189254
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993c, 1994), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)	Rombouts et al. (1988), Pitson et al. (1997)	*abfA*	P42254	An01g00330	206387
3.2.1.55	exo-α-L-arabinofuranosidase					An08g01710	38549
3.2.1.55	exo-α-L-arabinofuranosidase	vd Veen et al. (1991, 1993), Flipphi et al. (1993b), Ruijter et al. (1997), van Peij et al. (1998a), de Vries et al. (2002), de Groot et al. (2003)		*abfB*	P42255	An15g02300	200605
3.2.1.55	exo-α-L-arabinofuranosidase					An09g00880	131891
3.2.1.99	endo 1,5-α-L-arabinanase					An02g01400	134398
3.2.1.99	endo 1,5-α-L-arabinanase					An02g10550	197735
3.2.1.99	endo 1,5-α-L-arabinanase	vd Veen et al. (1991), Flipphi et al. (1993a), Ruijter et al. (1997), de Vries et al. (2002), de Groot et al. (2003)		*abnA*	P42256	An09g01190	203143
3.2.1.99	endo 1,5-α-L-arabinanase					An16g02730	184195
No EC	exo-arabinase	de Vries and Visser (2001)				N/A	N/A
3.2.1.23	β-galactosidase					An01g10350	46429
3.2.1.23	β-galactosidase					An06g00290	177434

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EC number	Name	Gene characterization	Details on the specificity	**Gene**	**Uniprot**	**CBS 513.88**	**ATCC 1015**
3.2.1.23	β-galactosidase					An07g04420	180727
3.2.1.23	β-galactosidase					An14g05820	41910
3.2.1.23	β-galactosidase	Kumar et al. (1992), de Vries et al. (1999a)		*lacA*	P29853	An01g12150	51764
3.2.1.89	β-1,4-endogalactanase					An16g06590	N/A
3.2.1.89	β-1,4-endogalactanase	Yamaguchi et al. (1995), de Vries et al. (2002a)	Yamaguchi et al. (1995), de Vries et al. (2002a)	*galA*	Q8X168	An18g05940	187227
3.1.1.73	Ferulic acid esterase A	Faulds and Williamson (1993), de Vries et al. (1997), van Peij et al. (1998a), de Vries et al. (1999b), de Vries and Visser (1999), Aliwan et al. (1999), de Vries et al. (2002)	Faulds and Williamson (1993), Aliwan et al. (1999)	*faeA*	O42807	An09g00120	51662
3.1.1.73	Ferulic acid esterase B	Kroon and Williamson (1996), de Vries et al. (2002)		*faeB*	Q8WZI8	N/A	51478

Table G.17: Literature on *A. niger* carbohydrate-active enzymes that could not be correlated to a specific gene.

EC number	Name	Enzyme characterization	Details on the specificity
3.1.1.11	pectin methylesterase		van Alebeek et al. (2003)
3.1.1.6	Acetyl esterase	Kormelink et al. (1993b), Linden et al. (1994)	Kormelink et al. (1993b)
3.1.1.73	cinnamate esterase	Barbe and Dubourdieu (1998)	
3.2.1.-	Xylosidase	Matsushita et al. (1985, 1987)	
3.2.1.131	α-glucuronidase	Uchida et al. (1992), Kiryu et al. (2005)	Kiryu et al. (2005)
3.2.1.15	endo-Polygalacturonase	Cooke et al. (1976), Kester and Visser (1990)	Kester and Visser (1990), Acuña-Argüelles et al. (1995), Singh and Appu Rao (2002)
3.2.1.21	β-glucosidase	Yan and Lin (1997), Adikane and Patil (1985), Alfani et al. (1987), Yeoh et al. (1988), Watanabe et al. (1992), Unno et al. (1993), Galas and Romanowska (1997), Xie et al. (2004)	Watanabe et al. (1992), Unno et al. (1993), Galas and Romanowska (1997), Xie et al. (2004)
3.2.1.22	α-galactosidase	Kaneko et al. (1991), Adya and Elbein (1977), Ademark et al. (2001b), Somiari and Balogh (1995)	Kaneko et al. (1991), Somiari and Balogh (1995)
3.2.1.23	β-galactosidase	Greenberg and Mahoney (1981), Bonnin et al. (1995)	
3.2.1.3	glucoamylase	Pazur et al. (1969), Freedberg et al. (1975)	
3.2.1.31	β-glucuronidase	Gottschalk et al. (1996)	
3.2.1.37	Xylan 1,4-β-xylosidase	Claeyssens et al. (1970), John et al. (1979), Rodionova et al. (1983)	
3.2.1.4	endo-glucanase	Vidmar et al. (1984), Singh et al. (1990b)	
3.2.1.40	α-L-rhamnosidase	Kurosawa et al. (1973)	
3.2.1.55	α-L-arabinofuranosidase	Kaji et al. (1969), Kaji and Tagawa (1970), Gunata et al. (1990), Waibel et al. (1980), Kaneko et al. (1993)	
3.2.1.67	exo-poly-D-galacturonase	Raab (1992), Heinrichova and Rexova-Benkova (1976)	Heinrichova and Rexova-Benkova (1976), Acuña-Argüelles et al. (1995), Limberg et al. (2000b), Sakamoto et al. (2002)
3.2.1.78	Endo-1,4-β-D-mannanase	Elbein et al. (1977), McCleary (1979), Regalado et al. (2000)	McCleary (1979)
3.2.1.8	Endo-(1,4)-β-xylanase	Gorbacheva and Rodionova (1977a,b), John et al. (1979), Frederick et al. (1981), Vrsanská et al. (1982), Biely et al. (1983), Frederick et al. (1985), Shei et al. (1985a,b), Meagher et al. (1988), Costa-Ferreira et al. (1994)	Frederick et al. (1981), Biely et al. (1983), Meagher et al. (1988)
3.2.1.89	β-1,4-endogalactanase	van de Vis et al. (1991)	van de Vis et al. (1991)
3.2.1.91	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase)	Singh et al. (1990a), Abdel-Naby et al. (1999)	
3.2.1.99	endo 1,5-α-L-arabinanase	Pitson et al. (1997)	
4.2.2.10	pectin lyase		Acuña-Argüelles et al. (1995), Limberg et al. (2000a)
No EC	rhamnogalacturonan acetylesterase	Rombouts et al. (1988)	
No EC	exo-β-1,3-galactanase	Pellerin and Brillouet (1994)	Pellerin and Brillouet (1994)
No EC	endo-β-1,6-galactanase	Brillouet et al. (1991)	

G.3 Maps of statistically significantly regulated genes

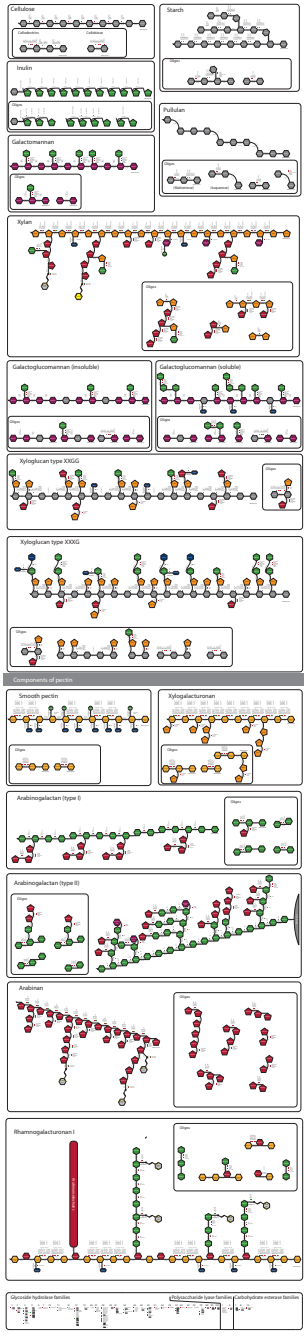

Figure G.16: Map of statistically significantly regulated genes coding for carbohydrate-active enzymes in a pairwise comparison of growth on arabinan versus arabinose. Genes marked with a red box are significantly up-regulated on arabinan relative to arabinose, a green box denotes the opposite, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence. The absence of a box mean that this gene is not statistically significantly regulated in this comparison.

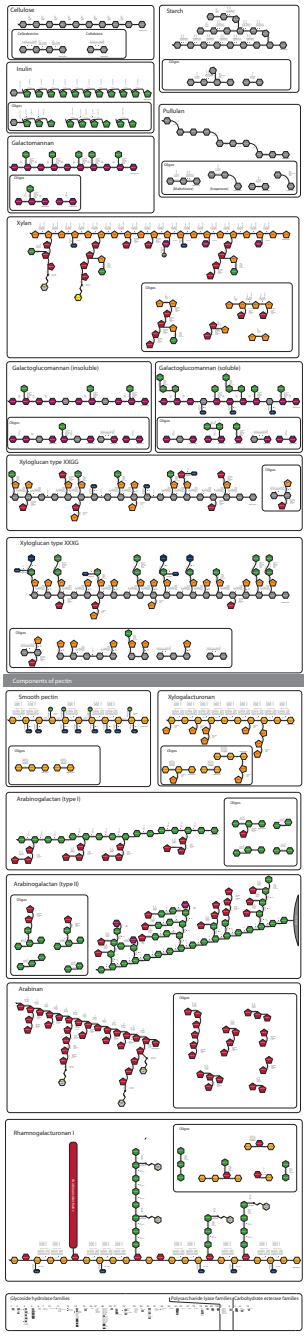

Figure G.17: Map of statistically significantly regulated genes coding for carbohydrate-active enzymes in a pairwise comparison of growth on starch versus glucose. Genes marked with a red box are significantly up-regulated on starch relative to glucose, a green box denotes the opposite, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence. The absence of a box mean that this gene is not statistically significantly regulated in this comparison.

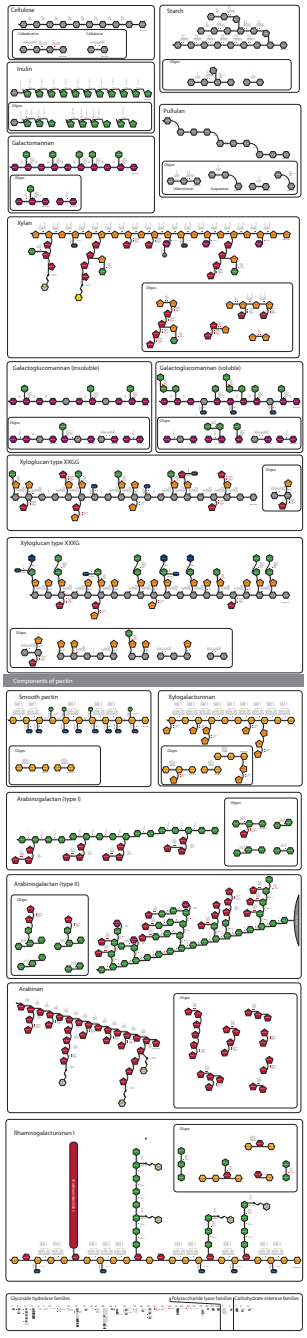

Figure G.18: Map of statistically significantly regulated genes coding for carbohydrate-active enzymes in a pairwise comparison of growth on arabinose versus glucose. Genes marked with a red box are significantly up-regulated on arabinose relative to glucose, a green box denotes the opposite, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence. The absence of a box mean that this gene is not statistically significantly regulated in this comparison.

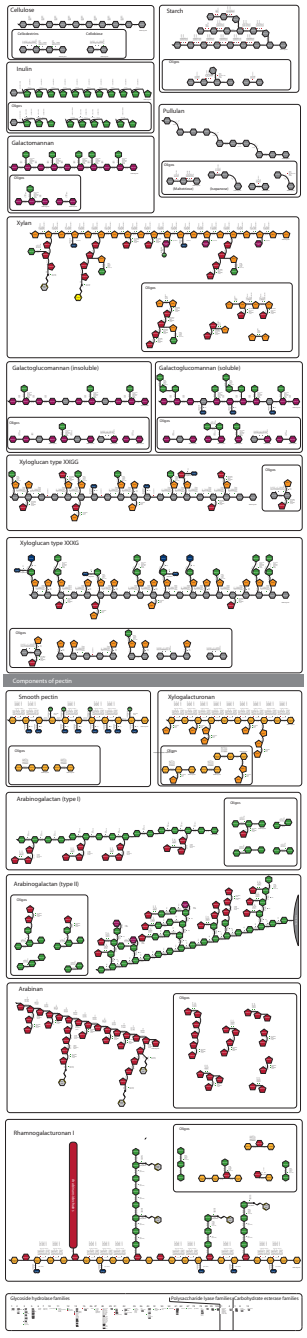

Figure G.19: Map of statistically significantly regulated genes coding for carbohydrate-active enzymes in a pairwise comparison of growth on arabinose versus glucose. Genes marked with a red box are significantly up-regulated on starch relative to xylan, a green box denotes the opposite, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence. The absence of a box mean that this gene is not statistically significantly regulated in this comparison.

G.4 Clustering of genes coding for carbohydrate enzymes

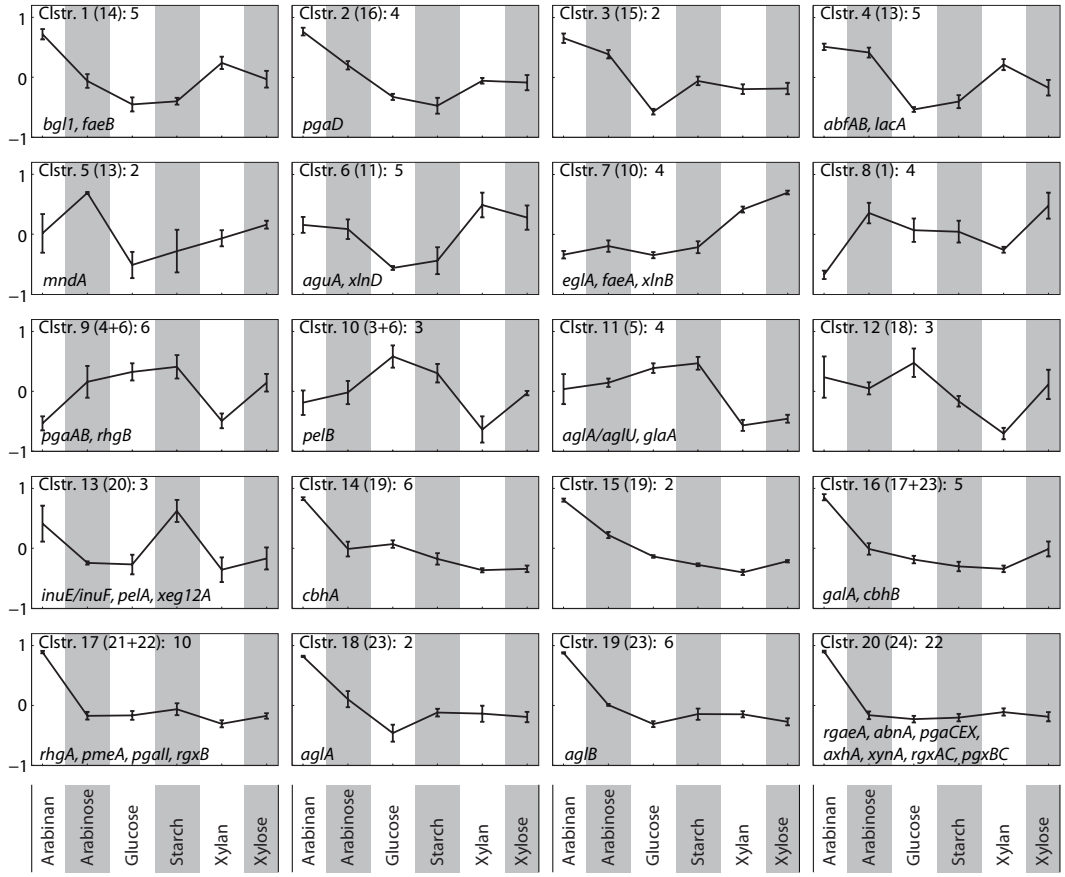

Figure G.20: Clustering of 103 significantly regulated genes coding for enzymes with putative and characterized polysaccharide-activities. All genes were found to be significantly regulated in at least one pairwise-comparison of two carbon sources. Cluster numbers in parentheses is the number of the corresponding cluster(s) in Figure 9.2. The number of genes in each cluster is shown next to the cluster number. The gene names of known genes found in a particular cluster are found at the bottom of the transcription profile graph of each cluster. The genes were clustered using the ClusterLustre algorithm (Grotkjaer et al., 2006).

Table G.18: Clustering results for genes coding for polysaccharide-acting enzymes. The first two columns are the gene IDs from the two *A. niger* genome sequencings. The genes are sorted according to clusters. A short description of the expression pattern is found in the Regulation column, while a summary term for the activity profile of the genes of the cluster is found in the Activity profile column (if one such existed

ATCC 1015	CBS 513.88	Cluster	Gene	Regulation	Activity profile
122069	An09g03110	1	α-amylase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
123981	An11g07660	1	candidate membrane bound β-glycosidase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
184195	An16g02730	1	endo 1,5-α-L-arabinanase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
211595	An12g04610	1	candidate endo-1,4-glucanase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
214608	An16g06800	1	candidate endoglucanase; C-terminal CBM1 module	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
38077	An08g08240	1	β-glucosidase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
39180	An11g06330	1	α-galactosidase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
40875	An15g07760	1	Endo-1,4-β-D-mannanase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
44520	An03g05330	1	β-glucosidase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
46827	An01g01260	1	β-glucuronidase	Up on mono-sugars and starch	Galactomannan and insoluble galactoglucomannan degradation
182162	An15g07800	2	α-amylase	Up on mono-sugars and starch	GH family 13.
191511	An03g05530	2	endo-glucanase	Up on mono-sugars and starch	GH family 13.
40878	An15g07810	2	candidate α-1,3-glucan synthase	Up on mono-sugars and starch	GH family 13.
54378	An09g03070	2	candidate α-1,3-glucan synthase	Up on mono-sugars and starch	GH family 13.
55204	An04g09890	2	membrane-bound α-1,3-glucan synthase (*agsA*);	Up on mono-sugars and starch	GH family 13.
128077	An07g04930	3	candidate membrane-bound α-glycosidase distantly related to endoarabinanases	Down on xylan	No clear profile
45304	An04g06930	3	α-amylase	Down on xylan	No clear profile
50378	An05g01320	3	Endo-1,4-β-D-mannanase	Down on xylan	No clear profile
53797	An14g02670	3	candidate endoglucanase; C-terminal CBM1 module	Down on xylan	No clear profile
178393	An11g06320	4	endo-rhamnogalacturonase	No clear regulation	No clear profile
180922	An07g01000	4	endo-rhamnogalacturonase	No clear regulation	No clear profile
210233	An15g04570	4	candidate β-glycosidase distantly related to endoglucanases; C-terminal CBM1 module	No clear regulation	No clear profile
52219	An02g04900	4	endo-Polygalacturonase (*pgaB*)	No clear regulation	No clear profile
119858	An01g10930	5	candidate α-glucosidase	Up on starch and glucose	Starch-degradation
140567	An11g03340	5	α-amylase	Up on starch and glucose	Starch-degradation
181816	An15g04800	5	β-glucosidase	Up on starch and glucose	Starch-degradation
213597	An03g06550	5	glucoamylase (exo-1,4-glucosidase/amyloglucosidase) (*glaA*)	Up on starch and glucose	Starch-degradation
214233	An04g06920	5	α-glucosidase (*aglA/aglU*)	Up on starch and glucose	Starch-degradation
206445	An02g00850	6	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)	Up on glucose and starch	α and β-glucan degradation and the pectin-backbone

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ATCC 1015	CBS 513.88	Cluster	Gene	Regulation	Gene profile
209376	An07g08950	6	endo-glucanase (*eglB*)	Up on glucose and starch	α and β-glucan degradation and the pectin-backbone
211163	An14g04200	6	rhamnogalacturonase B (*rhgB*)	Up on glucose and starch	α and β-glucan degradation and the pectin-backbone
214598	An16g06990	6	endo-Polygalacturonase (*pgaA*)	Up on glucose and starch	α and β-glucan degradation and the pectin-backbone
37060	An02g06950	6	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)	Up on glucose and starch	α and β-glucan degradation and the pectin-backbone
45821	An03g00190	6	pectin lyase (*pelB*)	Up on glucose and starch	α and β-glucan degradation and the pectin-backbone
123651	An06g02070	7	endo-Polygalacturonase (*(rhgC)*)	No clear regulation	Pectin-backbone degradation
182430	An15g04900	7	endo-glucanase	No clear regulation	Pectin-backbone degradation
208760	An11g04030	7	pectin lyase	No clear regulation	Pectin-backbone degradation
44977	An10g00290	7	candidate α-glycosidase related to bacterial α-L-rhamnosidases	No clear regulation	Pectin-backbone degradation
45021	An10g00870	7	pectate lyase A (*plyA*)	No clear regulation	Pectin-backbone degradation
134398	An02g01400	8	endo 1,5-α-L-arabinanase	Up on starch	Xylan-backbone degradation
141677	An01g11520	8	endo-Polygalacturonase (*pgaI*)	Up on starch	Xylan-backbone degradation
172587	An01g06630	8	β-mannosidase	Up on starch	Xylan-backbone degradation
176718	An08g09140	8	candidate α-glycosidase related to bacterial α-L-rhamnosidases	Up on starch	Xylan-backbone degradation
206333	An01g01870	8	endo-glucanase (*eglC*)	Up on starch	Xylan-backbone degradation
40261	An07g00350	8	α-glucosidase	Up on starch	Xylan-backbone degradation
52011	An01g03340	8	xyloglucan-specific endo-β-1,4-glucanase (*xeg12A*)	Up on starch	Xylan-backbone degradation
178172	An11g04040	9	exo-poly-D-galacturonase (*(pgxA)*)	Up on starch	Xylan-backbone degradation
189911	An12g03070	9	candidate α-glycosidase	Up on starch	Xylan-backbone degradation
55212	An19g00270	9	pectin lyase (*pelD*)	Up on starch	Xylan-backbone degradation
133986	An08g01760	10	endo-glucanase	Up on xylan, moreso on xylose	Xylan-active and with two endo-glucanases
211053	An14g02760	10	endo-glucanase (*eglA*)	Up on xylan, moreso on xylose	Xylan-active and with two endo-glucanases
43784	An12g02540	10	candidate β-glycosidase related to endoglucanases	Up on xylan, moreso on xylose	Xylan-active and with two endo-glucanases
46290	An01g13610	10	candidate α-glycosidase related to α-amylases and maltohexaose-forming α-amylases	Up on xylan, moreso on xylose	Xylan-active and with two endo-glucanases
51662	An09g00120	10	Ferulic acid esterase A (*faeA*)	Up on xylan, moreso on xylose	Xylan-active and with two endo-glucanases
52071	An01g00780	10	Endo-(1,4)-β-xylanase (*xynB/xlnB/xylB*)	Up on xylan, moreso on xylose	Xylan-active and with two endo-glucanases
176601	An06g02040	11	β-glucosidase	Up on arabinan, arabinose, xylan and xylose	Xylan exo-activities
205670	An01g09960	11	Xylan 1,4-β-xylosidase (*xlnD*)	Up on arabinan, arabinose, xylan and xylose	Xylan exo-activities
47677	An08g01900	11	Xylan 1,4-β-xylosidase	Up on arabinan, arabinose, xylan and xylose	Xylan exo-activities
56619	An14g05800	11	α-glucuronidase (*aguA*)	Up on arabinan, arabinose, xylan and xylose	Xylan exo-activities
131891	An09g00880	12	α-L-arabinofuranosidase	Up on xylan	No clear profile
188489	An09g03100	12	α-amylase	Up on xylan	No clear profile
210947	An14g01130	12	rhamnogalacturonan hydrolase (*rglA*)	Up on xylan	No clear profile
212736	An09g00260	12	α-galactosidase (*aglC*)	Up on xylan	No clear profile
54490	An12g02220	12	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase)	Up on xylan	No clear profile
138876	An11g06540	13	β-mannosidase (*mndA*)	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases
183088	An15g04550	13	Endo-(1,4)-β-xylanase	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases

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ATCC 1015	CBS 513.88	Cluster	Gene	Regulation	Gene profile
185285	An14g01800	13	α-galactosidase	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases
194447	An03g01050	13	endo-glucanase	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases
200605	An15g02300	13	α-L-arabinofuranosidase (*abfB*)	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases
206387	An01g00330	13	α-L-arabinofuranosidase (*abfA*)	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases
37673	An06g02460	13	candidate β-glycosidase distantly related to β-N-acetylglucosaminidases	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases
43342	An09g03300	13	related to α-glycosidases	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases
51764	An01g12150	13	β-galactosidase (*lacA*)	Up on xylan, arabinan and arabinose	Galactoglucomannan degradation and arabinofuranosidases
140573	An11g02100	14	candidate β-glycosidase; related to monolignol β-glucosidase	Up on xylan and arabinan	Removal of ferulic esters from arabinan and xylan
41703	An14g02920	14	related to rhamnogalacturonyl hydrolases	Up on xylan and arabinan	Removal of ferulic esters from arabinan and xylan
49940	An18g05620	14	candidate α-glycosidase	Up on xylan and arabinan	Removal of ferulic esters from arabinan and xylan
51478	An12g10390	14	Ferulic acid esterase B (*faeB*)	Up on xylan and arabinan	Removal of ferulic esters from arabinan and xylan
53702	An16g00540	14	candidate α-glycosidase distantly related to α-1,2-L-fucosidases	Up on xylan and arabinan	Removal of ferulic esters from arabinan and xylan
56782	An18g03570	14	β-glucosidase (*bgl1*)	Up on xylan and arabinan	Removal of ferulic esters from arabinan and xylan
122978	An08g10780	15	candidate β-glucosidase related to galactan 1,3-β-galactosidase; C-terminal CBM35 module	No clear regulation	No clear profile.
46065	An04g09700	15	endo-xylogalacturonan hydrolase	No clear regulation	No clear profile.
52928	An11g03200	15	endo-inulinase (*inuA/inuB*)	No clear regulation	No clear profile.
184037	An16g02760	16	candidate α-glycosidase distantly related to α-1,2-L-fucosidases	Up on arabinose and arabinan	No clear profile.
212893	An12g01850	16	candidate β-glycosidase related to bacterial β-mannosidases	Up on arabinose and arabinan	No clear profile.
38549	An08g01710	16	α-L-arabinofuranosidase	Up on arabinose and arabinan	No clear profile.
50161	An09g03260	16	endo-Polygalacturonase (*pgaD*)	Up on arabinose and arabinan	No clear profile.
52111	An02g00610	16	candidate β-glycosidase distantly related to β-glucuronidases	Up on arabinose and arabinan	No clear profile.
52452	An02g13240	16	candidate α-glycosidase related to α-glucosidases	Up on arabinose and arabinan	No clear profile.
182309	An15g01890	17	β-glucosidase	Up on arabinan	Cellulose-degradation
210716	An16g02100	17	candidate β-glycosidase	Up on arabinan	Cellulose-degradation
212915	An12g02450	17	candidate α-1,3-glucan synthase; N-terminal GH13 module and C-terminal GT5 module	Up on arabinan	Cellulose-degradation
45461	An16g09090	17	candidate membrane bound β-glycosidase related to β-N-acetylglucosaminidase	Up on arabinan	Cellulose-degradation
51773	An01g11660	17	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase) (*cbhB*)	Up on arabinan	Cellulose-degradation
57002	An12g02460	17	α-amylase	Up on arabinan	Cellulose-degradation

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ATCC 1015	CBS 513.88	Cluster	Gene	Regulation	Gene profile
120104	An02g07590	18	candidate β-glycosidase related to β-N-acetylhexosaminidase	No clear regulation	No clear profile.
210387	An15g07160	18	pectin lyase	No clear regulation	No clear profile.
213437	An03g03740	18	β-glucosidase	No clear regulation	No clear profile.
52811	An08g01100	18	candidate β-glycosidase related to exo-1,3-β-glucanases	No clear regulation	No clear profile.
128654	An09g05880	19	α-glucosidase	Up on arabinan	Cellulose-degradation
129891	An17g00520	19	β-glucosidase	Up on arabinan	Cellulose-degradation
175759	An06g02060	19	candidate β-glycosidase related to glucan 1,3-β-glucosidase	Up on arabinan	Cellulose-degradation
180727	An07g04420	19	β-galactosidase	Up on arabinan	Cellulose-degradation
190816	An04g02700	19	candidate α-glycosidase distantly related to plants alkaline α-galactosidases	Up on arabinan	Cellulose-degradation
194765	An04g08550	19	endo-glucanase	Up on arabinan	Cellulose-degradation
211162	An14g04190	19	candidate 1,4-α-glucan branching enzyme	Up on arabinan	Cellulose-degradation
39337	An11g08700	19	endo-rhamnogalacturonase	Up on arabinan	Cellulose-degradation
46621	An01g06120	19	candidate α-glycosidase related to glycogen-debranching enzyme	Up on arabinan	Cellulose-degradation
53159	An07g09330	19	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase) (*cbhA*)	Up on arabinan	Cellulose-degradation
205580	An01g11670	20	candidate endoglucanase; C-terminal CBM1 module	Up on starch and arabinan	No clear profile.
41815	An14g04370	20	pectin lyase (*pelA*)	Up on starch and arabinan	No clear profile.
44822	An13g02110	20	candidate α-glycosidase related to mammalian α-L-fucosidases	Up on starch and arabinan	No clear profile.
56664	An12g08280	20	exo-inulinase (*inuE/inuF/inu1*)	Up on starch and arabinan	No clear profile.
171269	An01g14600	21	Endo-(1,4)-β-xylanase	Up on arabinan	Xylan- and pectin-backbone activitities
182100	An15g03550	21	related to β-glycosidases	Up on arabinan	Xylan- and pectin-backbone activitities
182156	An15g05370	21	endo-Polygalacturonase (*pgaII*)	Up on arabinan	Xylan- and pectin-backbone activitities
189722	An12g00950	21	endo-Polygalacturonase (*rhgA*)	Up on arabinan	Xylan- and pectin-backbone activitities
43522	An09g01010	21	Acetylxylan esterase (*axeA*)	Up on arabinan	Xylan- and pectin-backbone activitities
52688	An08g05230	21	candidate endoglucanase	Up on arabinan	Xylan- and pectin-backbone activitities
187227	An18g05940	22	β-1,4-endogalactanase (*galA*)	Up on arabinan	No clear profile
194461	An03g02080	22	exo-poly-D-galacturonase ((*rgxB)*)	Up on arabinan	No clear profile
197735	An02g10550	22	endo 1,5-α-L-arabinanase	Up on arabinan	No clear profile
202490	An18g04100	22	candidate glucan 1,3-β-glucosidase	Up on arabinan	No clear profile
38924	An11g03120	22	Endo-(1,4)-β-xylanase	Up on arabinan	No clear profile
41877	An14g05340	22	distantly related to rhamnogalacturonyl hydrolases	Up on arabinan	No clear profile
50927	An13g03710	22	α-glucosidase	Up on arabinan	No clear profile
170172	An01g06620	23	candidate α-L-rhamnosidase	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
172232	An01g01320	23	α-galactosidase	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
189620	An05g02410	23	β-glucuronidase	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
207264	An02g11150	23	α-galactosidase (*aglB*)	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
210981	An14g01770	23	β-glucosidase	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
214857	An04g09690	23	pectin methylesterase	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
37736	An06g00170	23	α-galactosidase (*aglA*)	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
41910	An14g05820	23	β-galactosidase	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
46429	An01g10350	23	β-galactosidase	Up on arabinan	Exo-α- and β- galactosidase and glucosidase
51410	An04g09070	23	candidate α-L-rhamnosidase	Up on arabinan	Exo-α- and β- galactosidase and glucosidase

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ATCC 1015	CBS 513.88	Cluster	Gene	Regulation	Gene profile
131668	An12g05700	24	related to α-L-rhamnosidases	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
131747	An04g03170	24	β-glucosidase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
139037	An07g07630	24	β-glucosidase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
172236	An01g14650	24	exo-poly-D-galacturonase (*(rgxA)*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
172944	An02g12450	24	endo-Polygalacturonase (*(pgxC)*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
174379	An02g00140	24	Xylan 1,4-β-xylosidase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
176039	An06g02420	24	candidate β-glycosidase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
177434	An06g00290	24	β-galactosidase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
179265	An11g00200	24	candidate β-glucosidase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
189254	An09g02160	24	rhamnogalacturonan acetylesterase (*rgaeA*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
191158	An03g06740	24	exo-poly-D-galacturonase (*(pgxB)*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
198063	An08g11070	24	candidate invertase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
203143	An09g01190	24	endo 1,5-α-L-arabinanase (*abnA*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
208871	An11g06080	24	β-glucosidase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
36414	An01g01340	24	candidate glycosidase related to a bacterial d-4,5 unsaturated glucuronyl hydrolase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
40264	An07g00240	24	candidate α-glycosidase related to bacterial α-L-rhamnosidases	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
42184	An12g07500	24	exo-poly-D-galacturonase (*(pgaX)*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
42916	An18g04800	24	candidate membrane-bound α-glycosidase related to α-L-rhamnosidases	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
42917	An18g04810	24	exo-poly-D-galacturonase (*(rgxC)*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
43957	An05g02440	24	endo-Polygalacturonase (*pgaC*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
44585	An03g06310	24	pectin methylesterase (*pmeA*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
46255	An01g14670	24	endo-Polygalacturonase (*pgaE*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
50997	An17g00300	24	candidate β-glycosydase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
55136	An03g00960	24	α-L-arabinofuranosidase (*axhA*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation
55419	An01g04880	24	α-glucosidase	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation

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ATCC 1015	CBS 513.88	Cluster	Gene	Regulation	Gene profile
57436	An03g00940	24	Endo-(1,4)-β-xylanase (*xynA*)	Up on arabinan	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation

Table G.19: Clustering results for significantly regulated genes coding for polysaccharide-acting enzymes. The first two columns are the gene IDs from the two genome sequencings. The genes are sorted according to clusters. The "Similar to"-column refers to which cluster of App. Table G.18/Figure 9.2 the cluster in this table is similar to. A short description of the expression pattern is found in the Regulation column, while a summary term for the activity profile of the genes of the cluster is found in the Activity profile column (if one such existed

ATCC 1015	CBS 513.88	Cluster	Similar to	Gene	Regulation	Gene profile
140573	An11g02100	1	14	candidate β-glycosidase; related to monolignol β-glucosidase	Removal of ferulic esters from arabinan and xylan	Up on xylan and arabinan
41703	An14g02920	1	14	related to rhamnogalacturonyl hydrolases	Removal of ferulic esters from arabinan and xylan	Up on xylan and arabinan
51478	An12g10390	1	14	Ferulic acid esterase B (*faeB*)	Removal of ferulic esters from arabinan and xylan	Up on xylan and arabinan
53702	An16g00540	1	14	candidate α-glycosidase distantly related to α-1,2-L-fucosidases	Removal of ferulic esters from arabinan and xylan	Up on xylan and arabinan
56782	An18g03570	1	14	β-glucosidase (*bgl1*)	Removal of ferulic esters from arabinan and xylan	Up on xylan and arabinan
184037	An16g02760	2	16	candidate α-glycosidase distantly related to α-1,2-L-fucosidases	No clear profile.	Up on arabinose and arabinan
212893	An12g01850	2	16	candidate β-glycosidase related to bacterial β-mannosidases	No clear profile.	Up on arabinose and arabinan
38549	An08g01710	2	16	α-L-arabinofuranosidase	No clear profile.	Up on arabinose and arabinan
50161	An09g03260	2	16	endo-Polygalacturonase (*pgaD*)	No clear profile.	Up on arabinose and arabinan
122978	An08g10780	3	15	candidate β-glucosidase related to galactan 1,3-b-galactosidase; C-terminal CBM35 module	No clear profile.	No clear regulation
46065	An04g09700	3	15	endo-xylogalacturonan hydrolase	No clear profile.	No clear regulation
185285	An14g01800	4	13	α-galactosidase	Galactoglucomannan degradation and arabinofuranosidases	Up on xylan, arabinan and arabinose
194447	An03g01050	4	13	endo-glucanase	Galactoglucomannan degradation and arabinofuranosidases	Up on xylan, arabinan and arabinose
200605	An15g02300	4	13	α-L-arabinofuranosidase (*abfB*)	Galactoglucomannan degradation and arabinofuranosidases	Up on xylan, arabinan and arabinose
206387	An01g00330	4	13	α-L-arabinofuranosidase (*abfA*)	Galactoglucomannan degradation and arabinofuranosidases	Up on xylan, arabinan and arabinose
51764	An01g12150	4	13	β-galactosidase (*lacA*)	Galactoglucomannan degradation and arabinofuranosidases	Up on xylan, arabinan and arabinose
138876	An11g06540	5	13	β-mannosidase (*mndA*)	No clear profile	Up on xylan, arabinan and arabinose
183088	An15g04550	5	13	Endo-(1,4)-β-xylanase	No clear profile	Up on xylan, arabinan and arabinose
188489	An09g03100	6	11	α-amylase	Xylan exo-activities	Up on arabinan, arabinose, xylan and xylose
205670	An01g09960	6	11	Xylan 1,4-β-xylosidase (*xlnD*)	Xylan exo-activities	Up on arabinan, arabinose, xylan and xylose
43342	An09g03300	6	11	related to α-glycosidases	Xylan exo-activities	Up on arabinan, arabinose, xylan and xylose
47677	An08g01900	6	11	Xylan 1,4-β-xylosidase	Xylan exo-activities	Up on arabinan, arabinose, xylan and xylose
56619	An14g05800	6	11	α-glucuronidase (*aguA*)	Xylan exo-activities	Up on arabinan, arabinose, xylan and xylose
211053	An14g02760	7	10	endo-glucanase (*eglA*)	Xylan-active enzymes	Up on xylan, moreso on xylose

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ATCC 1015	CBS 513.88	Cluster	Similar to	Gene	Regulation	Gene profile
46290	An01g13610	7	10	candidate α-glycosidase related to α-amylases and maltohexaose-forming α-amylases	Xylan-active enzymes	Up on xylan, moreso on xylose
51662	An09g00120	7	10	Ferulic acid esterase A (*faeA*)	Xylan-active enzymes	Up on xylan, moreso on xylose
52071	An01g00780	7	10	Endo-(1,4)-β-xylanase (*xynB/xlnB/xylB*)	Xylan-active enzymes	Up on xylan, moreso on xylose
122069	An09g03110	8	1	α-amylase	No clear profile.	Arabinan down and Xylose up
184195	An16g02730	8	1	endo 1,5-α-L-arabinanase	No clear profile.	Arabinan down and Xylose up
214608	An16g06800	8	1	candidate endoglucanase; C-terminal CBM1 module	No clear profile.	Arabinan down and Xylose up
44520	An03g05330	8	1	β-glucosidase	No clear profile.	Arabinan down and Xylose up
191511	An03g05530	9	4 and 6	endo-glucanase	Endo-acting enzymes	Induced by high sugar-concentrations
210233	An15g04570	9	4 and 6	candidate β-glycosidase distantly related to endoglucanases; C-terminal CBM1 module	Endo-acting enzymes	Induced by high sugar-concentrations
211163	An14g04200	9	4 and 6	rhamnogalacturonase B (*rhgB*)	Endo-acting enzymes	Induced by high sugar-concentrations
214598	An16g06990	9	4 and 6	endo-Polygalacturonase (*pgaA*)	Endo-acting enzymes	Induced by high sugar-concentrations
52219	An02g04900	9	4 and 6	endo-Polygalacturonase (*pgaB*)	Endo-acting enzymes	Induced by high sugar-concentrations
55204	An04g09890	9	4 and 6	membrane-bound α-1,3-glucan synthase (EC 2.4.1.183); N-terminal GH13 module and C-terminal GT5 module	Endo-acting enzymes	Induced by high sugar-concentrations
206445	An02g00850	10	3 and 6	glucoamylase (exo-1,4-glucosidase/amyloglucosidase)	Amylases and pectin lyase	Up on glucose and starch, down on xylan
45304	An04g06930	10	3 and 6	α-amylase	Amylases and pectin lyase	Up on glucose and starch, down on xylan
45821	An03g00190	10	3 and 6	pectin lyase (*pelB*)	Amylases and pectin lyase	Up on glucose and starch, down on xylan
119858	An01g10930	11	5	candidate α-glucosidase	Starch-degradation	Up on starch and glucose
140567	An11g03340	11	5	α-amylase	Starch-degradation	Up on starch and glucose
213597	An03g06550	11	5	glucoamylase (exo-1,4-glucosidase/amyloglucosidase) (*glaA*)	Starch-degradation	Up on starch and glucose
214233	An04g06920	11	5	α-glucosidase (*aglA/aglU*)	Starch-degradation	Up on starch and glucose
120104	An02g07590	12	18	candidate β-glycosidase related to β-N-acetylhexosaminidase	No clear profile.	No clear regulation
210387	An15g07160	12	18	pectin lyase	No clear profile.	No clear regulation
54378	An09g03070	12	18	candidate α-1,3-glucan synthase; N-terminal GH13 module and C-terminal GT5 module	No clear profile.	No clear regulation
41815	An14g04370	13	20	pectin lyase (*pelA*)	Pectin lyases and glucanases/glucosidases	Up on starch and arabinan
52011	An01g03340	13	20	xyloglucan-specific endo-β-1,4-glucanase (*xeg12A*)	Pectin lyases and glucanases/glucosidases	Up on starch and arabinan
56664	An12g08280	13	20	exo-inulinase (*inuE/inuF/inu1*)	Pectin lyases and glucanases/glucosidases	Up on starch and arabinan
128654	An09g05880	14	19	α-glucosidase	Glucans and glucosidases	Up on arabinan and glucose
129891	An17g00520	14	19	β-glucosidase	Glucans and glucosidases	Up on arabinan and glucose
190816	An04g02700	14	19	candidate α-glycosidase distantly related to plants alkaline α-galactosidases	Glucans and glucosidases	Up on arabinan and glucose
194765	An04g08550	14	19	endo-glucanase	Glucans and glucosidases	Up on arabinan and glucose
211162	An14g04190	14	19	candidate 1,4-a-glucan branching enzyme	Glucans and glucosidases	Up on arabinan and glucose
53159	An07g09330	14	19	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase) (*cbhA*)	Glucans and glucosidases	Up on arabinan and glucose
39337	An11g08700	15	19	endo-rhamnogalacturonase	No clear profile	Up on arabinan
46621	An01g06120	15	19	candidate α-glycosidase related to glycogen-debranching enzyme	No clear profile	Up on arabinan

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ATCC 1015	CBS 513.88	Cluster	Similar to	Gene	Regulation	Gene profile
170172	An01g06620	16	17 and 23	candidate α-L-rhamnosidase	Cellulose-degradation and rhamnosidases	Up on arabinan
187227	An18g05940	16	17 and 23	β-1,4-endogalactanase (*galA*)	Cellulose-degradation and rhamnosidases	Up on arabinan
210716	An16g02100	16	17 and 23	candidate β-glycosidase	Cellulose-degradation and rhamnosidases	Up on arabinan
51410	An04g09070	16	17 and 23	candidate α-L-rhamnosidase	Cellulose-degradation and rhamnosidases	Up on arabinan
51773	An01g11660	16	17 and 23	Cellulose 1,4-β-cellobiosidase (Cellobiohydrolase) (*cbhB*)	Cellulose-degradation and rhamnosidases	Up on arabinan
182156	An15g05370	17	21-22	endo-Polygalacturonase (*pgaII*)	Xylan- and pectin-backbone activities	Up on arabinan
189722	An12g00950	17	21-22	endo-Polygalacturonase (*rhgA*)	Xylan- and pectin-backbone activities	Up on arabinan
194461	An03g02080	17	21-22	exo-poly-D-galacturonase ((*rgxB*))	Xylan- and pectin-backbone activities	Up on arabinan
197735	An02g10550	17	21-22	endo 1,5-α-L-arabinanase	Xylan- and pectin-backbone activities	Up on arabinan
202490	An18g04100	17	21-22	candidate glucan 1,3-β-glucosidase	Xylan- and pectin-backbone activities	Up on arabinan
38924	An11g03120	17	21-22	Endo-(1,4)-β-xylanase	Xylan- and pectin-backbone activities	Up on arabinan
41877	An14g05340	17	21-22	distantly related to rhamnogalacturonyl hydrolases	Xylan- and pectin-backbone activities	Up on arabinan
44585	An03g06310	17	21-22	pectin methylesterase (*pmeA*)	Xylan- and pectin-backbone activities	Up on arabinan
50927	An13g03710	17	21-22	α-glucosidase	Xylan- and pectin-backbone activities	Up on arabinan
52688	An08g05230	17	21-22	candidate endoglucanase	Xylan- and pectin-backbone activities	Up on arabinan
207264	An02g11150	18	23	α-galactosidase (*aglB*)	No clear profile	Up on arabinan
214857	An04g09690	18	23	pectin methylesterase	No clear profile	Up on arabinan
172232	An01g01320	19	23	α-galactosidase	Exo-α- and β-galactosidase and α- and β-glucosidase	Up on arabinan
189620	An05g02410	19	23	β-glucuronidase	Exo-α- and β-galactosidase and α- and β-glucosidase	Up on arabinan
210981	An14g01770	19	23	β-glucosidase	Exo-α- and β-galactosidase and α- and β-glucosidase	Up on arabinan
37736	An06g00170	19	23	α-galactosidase (*aglA*)	Exo-α- and β-galactosidase and α- and β-glucosidase	Up on arabinan
41910	An14g05820	19	23	β-galactosidase	Exo-α- and β-galactosidase and α- and β-glucosidase	Up on arabinan
46429	An01g10350	19	23	β-galactosidase	Exo-α- and β-galactosidase and α- and β-glucosidase	Up on arabinan
131668	An12g05700	20	24	related to α-L-rhamnosidases	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
131747	An04g03170	20	24	β-glucosidase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan

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ATCC 1015	CBS 513.88	Cluster	Similar to	Gene	Regulation	Gene profile
172236	An01g14650	20	24	exo-poly-D-galacturonase ((*rgxA*))	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
172944	An02g12450	20	24	endo-Polygalacturonase ((*pgxC*))	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
174379	An02g00140	20	24	Xylan 1,4-β-xylosidase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
177434	An06g00290	20	24	β-galactosidase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
179265	An11g00200	20	24	candidate β-glucosidase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
189254	An09g02160	20	24	rhamnogalacturonan acetylesterase (*rgaeA*)	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
191158	An03g06740	20	24	exo-poly-D-galacturonase ((*pgxB*))	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
198063	An08g11070	20	24	candidate invertase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
203143	An09g01190	20	24	endo 1,5-α-L-arabinanase (*abnA*)	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
208871	An11g06080	20	24	β-glucosidase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
36414	An01g01340	20	24	candidate glycosidase related to a bacterial d-4,5 unsaturated glucuronyl hydrolase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
42184	An12g07500	20	24	exo-poly-D-galacturonase ((*pgaX*))	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
42916	An18g04800	20	24	candidate membrane-bound α-glycosidase related to α-L-rhamnosidases	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
42917	An18g04810	20	24	exo-poly-D-galacturonase ((*rgxC*))	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
43957	An05g02440	20	24	endo-Polygalacturonase (*pgaC*)	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
46255	An01g14670	20	24	endo-Polygalacturonase (*pgaE*)	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
50997	An17g00300	20	24	candidate β-glycosidase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan

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ATCC 1015	CBS 513.88	Cluster	Similar to	Gene	Regulation	Gene profile
55136	An03g00960	20	24	α-L-arabinofuranosidase (*axhA*)	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
55419	An01g04880	20	24	α-glucosidase	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan
57436	An03g00940	20	24	Endo-(1,4)-β-xylanase (*xynA*)	Rhamnogalacturonan I, smooth pectin and xylogalacturonan degradation	Up on arabinan

G.5 Maps of gene clusters

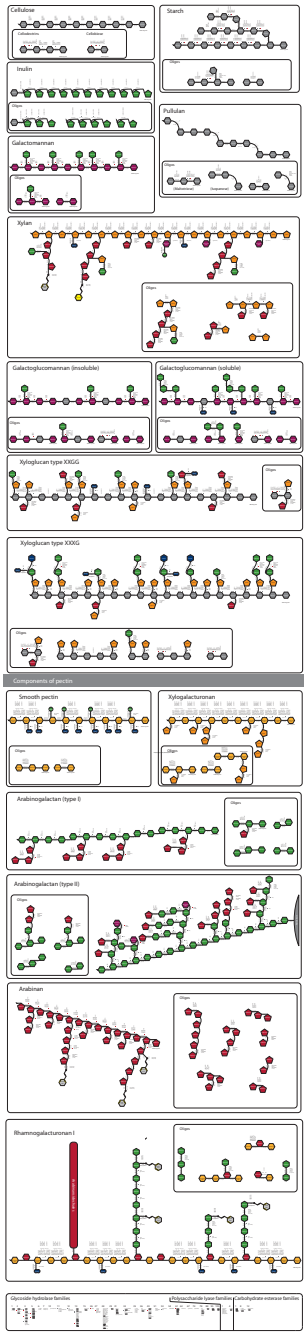

Figure G.21: Map of co-regulated genes of cluster 1. Genes marked with a red box are found in the cluster, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence.

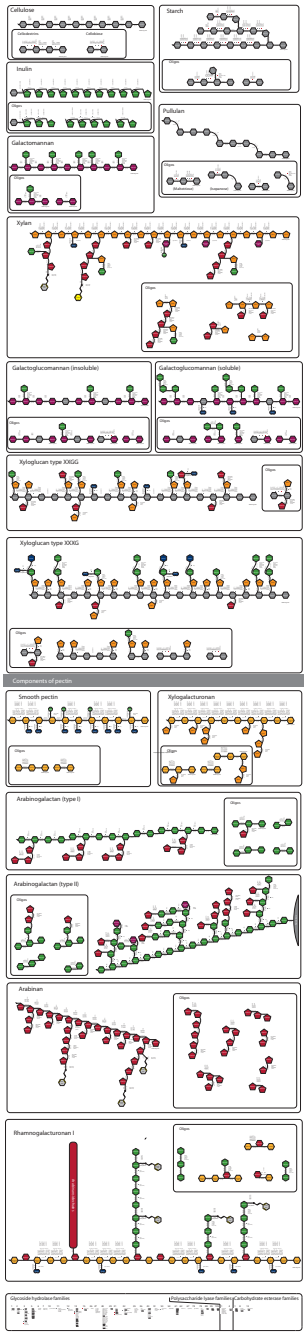

Figure G.22: Map of co-regulated genes of cluster 5. Genes marked with a red box are found in the cluster, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence.

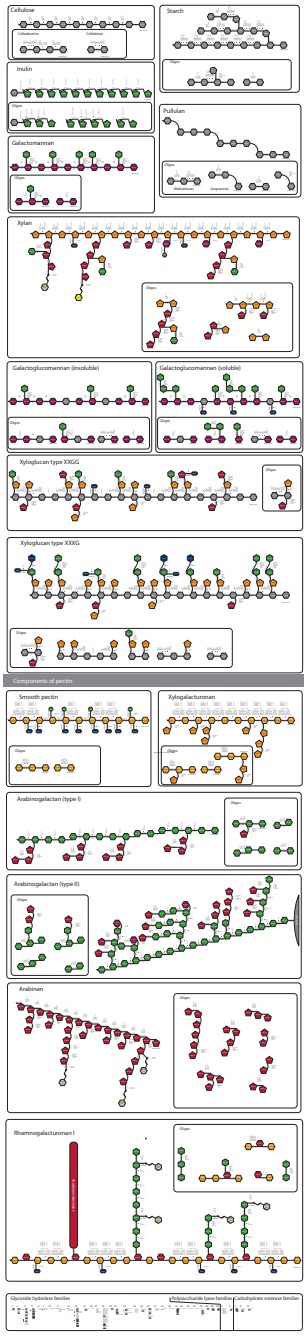

Figure G.23: Map of co-regulated genes of cluster 17. Genes marked with a red box are found in the cluster, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence.

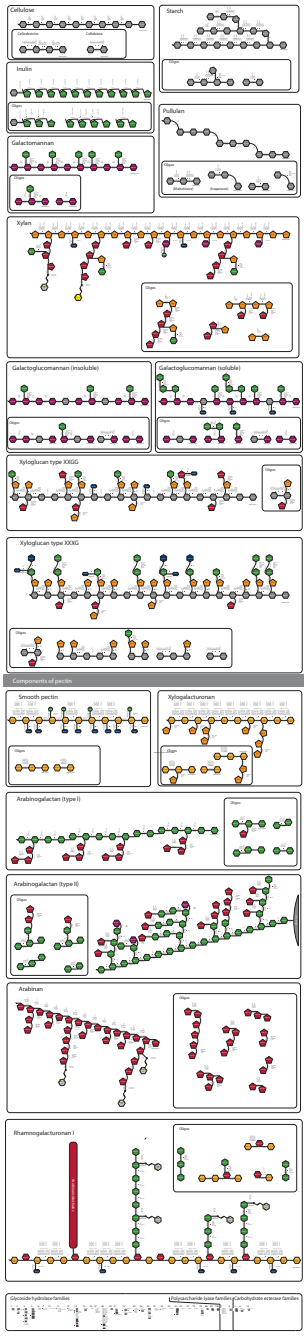

Figure G.24: Map of co-regulated genes of cluster 19. Genes marked with a red box are found in the cluster, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence.

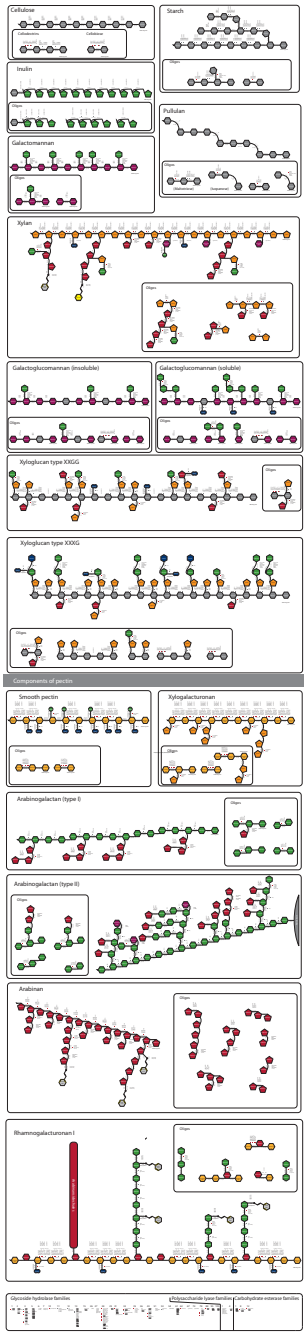

Figure G.25: Map of co-regulated genes of cluster 24. Genes marked with a red box are found in the cluster, gray boxes means that the gene is found in the *A. niger* CBS 513.88 sequence, but no bi-directional best hit is found in the *A. niger* ATCC 1015 sequence.